NASA

National Aeronautics and
Space Administration

May 24, 1996

NRA-96-OLMSA-03

RESEARCH ANNOUNCEMENT

Microgravity Biotechnology: Research and Flight Experiment Opportunities

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Letters of Intent Due: ..... July 19, 1996

Proposals Due: ..... August 27, 1996

OMB Approval No. 2700-0087

MICROGRAVITY BIOTECHNOLOGY: RESEARCH AND FLIGHT EXPERIMENT OPPORTUNITIES

NASA Research Announcement
Soliciting Research Proposals
for the Period Ending
August 27, 1996

NRA-96-OLMSA-03
Issued: May 24, 1996

Office of Life and Microgravity Sciences and Applications
National Aeronautics and Space Administration
Washington, D.C. 20546-0001

NASA RESEARCH ANNOUNCEMENT
MICROGRAVITY BIOTECHNOLOGY:
RESEARCH AND FLIGHT EXPERIMENT OPPORTUNITIES

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NASA RESEARCH ANNOUNCEMENT

MICROGRAVITY BIOTECHNOLOGY: RESEARCH AND FLIGHT EXPERIMENT OPPORTUNITIES

This NASA Research Announcement (NRA) solicits research proposals to conduct scientific investigations in the discipline of microgravity biotechnology. These investigations may involve flight experiments or ground-based experimental and theoretical research intended to support the study of biotechnology using the low-gravity environment of space. Flight experiments may be proposed that develop new instruments or use existing instruments described in this solicitation. Descriptions of the technical areas of interest under this research announcement appear in Appendix A.

Investigations selected for flight experiment definition must successfully complete a number of subsequent development steps, including peer review of the flight experiment, in order to be considered for a flight assignment. NASA does not guarantee that any investigation selected for definition will advance to flight experiment status.

Participation is open to U.S. industry, educational institutions, other nonprofit organizations, NASA research centers, other U.S. Government agencies, and to international investigations. In the case of international investigations, NASA can only fund U.S. investigators involved in the investigation (see Additional Guidelines for International Participation, Appendix A, Section V).

Proposals must be submitted before August 27, 1996, 4:30 PM EDT. NASA reserves the right to consider proposals received after that date if such action is judged to be in the best interests of the Government. Proposals will be evaluated by scientific peer review and, if appropriate, engineering feasibility reviews. Selections are planned to be announced in April 1997.

Appendices A and B provide technical and program information applicable only to this NRA. Appendix C contains general guidelines for the preparation of proposals solicited by an NRA.

This Announcement is part of a planned sequence of solicitations inviting proposals in the disciplines of the microgravity program.

NASA Research Announcement Identifier: NRA-96-OLMSA-03
Letters of Intent Due: July 19, 1996. Proposals Due: August 27, 1996

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If electronic means are not available, you may mail Letters of Intent to the address given below.

Submit Proposals to the following address:

NASA c/o Information Dynamics Inc.
Subject: NASA Research Proposal (NRA-96-OLMSA-03)
300 D Street, S.W., Suite 801
Washington, D.C. 20024
Telephone number for delivery services: (202) 479-2609

Proposal Copies Required:.....15

Proposers will receive a postcard confirming receipt of proposal within 10 working days of the due date.

Obtain Additional Information at the following address:

Dr. Stephen Davison
Microgravity Science and Applications Division
Code UG
National Aeronautics and Space Administration
300 E Street, S.W.
Washington, D.C. 20546-0001
(202) 358-0813

Selecting Official: ..... Director
Microgravity Science and Applications Division
Office of Life and Microgravity Sciences
and Applications

Your interest and cooperation in participating in this effort are appreciated.

Arnauld E. Nicogossian, M.D.
Acting Associate Administrator for
Life and Microgravity Sciences and Applications

Technical Description

**MICROGRAVITY BIOTECHNOLOGY:
RESEARCH AND FLIGHT EXPERIMENT OPPORTUNITIES**

I. INTRODUCTION

A. BACKGROUND

The National Aeronautics and Space Administration (NASA) conducts a program of basic and applied research using the reduced-gravity environment to improve the understanding of fundamental physical, chemical, and biological processes. The scope of the program sponsored by the Microgravity Science and Applications Division (MSAD) ranges from applied research into the effects of low-gravity on chemical, biological, and physical processes to basic research that uses low-gravity to probe the fundamental behavior of matter. This announcement is part of an ongoing effort to develop research in a specific scientific discipline, Microgravity Biotechnology. The biotechnology discipline is a growing focus of the microgravity science and applications program. The Division last released a NASA Research Announcement (NRA) for biotechnology in 1994 and expects to continue to release NRA's in biotechnology approximately every two years.

In the MSAD program, ground-based research has been used to gain a preliminary understanding of phenomena, and to define experiments to be conducted in the extended low-gravity test times available in spacecraft in low Earth orbit. MSAD anticipates flight opportunities for new Shuttle and early Space Station research instruments. MSAD is currently studying the development of modular research instruments that can be configured (or reconfigured) to accommodate multiple experiments and multiple users. This is envisioned as an evolutionary program with the objectives of providing experimental data in response to increasingly sophisticated science requirements and of permitting the evolution of experimental approaches and technologies as needed for scientific investigations throughout the era of Space Station. This announcement is being released as part of a coordinated series of discipline-directed solicitations intended to span the range of the MSAD program. Other solicitations planned, as is this one, for periodic release over the next several years include:

Fluid Physics
Low Temperature Physics
Combustion Science
Materials Science.

The scope of this research announcement does not include research dealing with the response of living organisms to weightlessness, an area which is the focus of an ongoing program in the Life and Biomedical Sciences and Applications Division.

The Office of Space Access and Technology (OSAT), Space Processing Division encourages proposers to address objectives in commercial research. Please see the attachment at the back of this NRA (Notice of Areas of Interest for Biotechnology Applied Research for the Commercial Development of Space Program) for information on opportunities that exist for proposals which predominantly feature applied commercial research and must have an industrial, cost sharing partner. This attachment is for informational purposes and is not part of this NASA Research Announcement (NRA).

B. RESEARCH ANNOUNCEMENT OBJECTIVES

This NRA has the objective of broadening and enhancing the MSAD microgravity biotechnology program, the goals of which are described in Section II, through the solicitation of:

1. Experimental studies which require the space environment to test clearly posed hypotheses, using existing or slightly modified instruments in space-based experiments to increase the understanding of biotechnology;

2. Experiment concepts which will define and utilize new instruments for space-based experiments in biotechnology; and

3. Ground-based theoretical and experimental studies which will lead to the definition or enhance the understanding of existing or potential flight experiments in biotechnology.

Further programmatic objectives of this NRA include those objectives broadly emphasized by the civil space program, including: the advancement of economically significant technologies; technology infusement into the private sector; and enhancement of the diversity of participation in the space program, and several objectives of specific importance to the microgravity science and applications program. These latter objectives include the support of investigators in early stages of their careers, with the purpose of developing a community of established researchers for the International Space Station and other missions in the next 10-20 years, and the pursuit of microgravity research that will contribute to economically significant advances in technology.

C. DESCRIPTION OF THE ANNOUNCEMENT

With this NRA, NASA is soliciting proposals to conduct research in microgravity biotechnology, with an emphasis on experimental efforts that are sufficiently mature to justify near-term flight development. The goals of the discipline along with some identified research areas of interest are described in Section II. Proposals describing innovative low-gravity biotechnology research beyond that described are also sought.

NASA is currently developing several types of flight instruments for microgravity biotechnology research. Brief descriptions of the planned capabilities are given in Appendix B, Section I. NASA anticipates several near-term flight opportunities for investigations with requirements which can be met by existing apparatus with only minor modifications. Successful proposals for use of the existing apparatus will be funded for definition studies which will produce a detailed Science Requirements Document (SRD). Authorization to proceed into flight development is contingent upon successful peer review of the experiment and SRD by both science and engineering panels. NASA does not guarantee that any experiment selected for definition which plans to use existing hardware will advance to flight experiment status.

NASA also encourages submission of experiment proposals for which none of the existing flight instruments are appropriate. NASA anticipates the development of new biotechnology research experiment apparatus for use in the Space Station era. Selected proposals requiring development of new capabilities will be funded for definition studies to determine flight experiment parameters and conditions and the appropriate flight hardware. The length of the definition phase will be based on the experiment requirements, but will normally range from 6 to 24 months and will culminate in the preparation of an SRD. Authorization to proceed into flight development is contingent upon successful peer review of the SRD by both science and engineering panels. NASA does not guarantee that any experiment selected for definition which requires new instrument development will advance to flight experiment status.

Investigations that do not proceed into flight development will normally be asked to submit a proposal for continuation of support at the conclusion of a typical four-year period of funding. Promising proposals which are not mature enough to allow development of a flight concept within two years of definition may be selected for support in the MSAD Research and Analysis (R&A) Program. Investigations selected into the R&A program must generally propose again to a future announcement in order to be selected for a flight opportunity.

II. MICROGRAVITY BIOTECHNOLOGY RESEARCH

A. INTRODUCTION

Use of the microgravity environment is just beginning to increase our understanding of the biological sciences and to enable us to develop innovative biotechnological processes that can exploit space. There is abundant practical motivation for advancing biotechnology; it plays a key role in health, agriculture, and many other important economic areas. Advances in biotechnology will benefit a wide range of applications and research areas which depend on biotechnology as a basis for their work.

The NASA biotechnology program has identified protein crystal growth, biotechnology cell science, and fundamentals of biotechnology as areas which contain promising opportunities for significant advancements through low-gravity experiments. Therefore, under this announcement, NASA is requesting proposals for research in these areas. Innovative proposals in areas of biotechnology not specified in this announcement that show a clear indication that they are affected by low gravity will also be accepted.

B. MICROGRAVITY BIOTECHNOLOGY GOALS AND DESCRIPTION OF PARTICIPATION

The biotechnology program seeks a coordinated research effort involving both space- and ground-based research. The overall goal of the biotechnology program of the Microgravity and Science Applications Division (MSAD) of NASA is to use the low-gravity environment to support novel biotechnology research. The individual goals are 1) to advance the scientific understanding of biotechnology processes affected by gravity, 2) to use low-gravity experiments for insight into the physical behavior of biotechnology processes, 3) to provide the scientific knowledge needed to improve these processes, 4) to contribute to Earth-based systems concerned with biotechnology, and 5) to develop technologies specifically supporting low-gravity experiments and practical aspects in biotechnology.

To accomplish these goals, this research announcement is soliciting two types of proposals for all areas of microgravity biotechnology research:

I) Flight proposals to carry out experimental research in the space environment

– Experimental studies which require the space environment to test clearly posed hypotheses, using existing or slightly modified instruments in space-based experiments to increase the understanding of biotechnology.

– Experiment concepts which will define and utilize new instruments for space-based experiments in biotechnology.

II) Ground-based experimental and theoretical research proposals

– Ground-based theoretical and experimental studies which will lead to the definition or enhance the understanding of existing or potential flight experiments in biotechnology.

C. BIOTECHNOLOGY CELL SCIENCE

Introduction

NASA's cell research has focused on the development of rotating vessel bioreactors for the culture of cells using well-controlled process parameters and reduced levels of hydrodynamic stress, thus simulating the low gravity conditions of space to the extent possible on Earth. Using these rotating vessel bioreactors researchers have achieved three-dimensional tissue propagation in an aqueous medium. To further develop this technology and support research in this area, NASA is developing a program to understand the role of reduced hydrodynamic stress and spatial co-location on mammalian tissue adhesion, proliferation, and eventual differentiation (1). Research in this area will help establish the scientific basis for conducting culture

experiments in the microgravity environment of space, contribute to the culture of functional and differentiated tissues for use in medical treatments, and will contribute to advances in developmental biology. The microgravity environment affords a unique opportunity to culture cells because they may be grown in three-dimensions in aqueous media without sedimentation. This provides the opportunity to recreate the three-dimensional relationships among cells that are extremely important to normal organ function. At this point, the research program has established a cadre of investigators who are involved in ground-based research on the feasibility of low gravity culture systems.

Millions of Americans suffer tissue or organ loss from diseases and accidents every year, and the yearly cost of treating these patients exceeds $400 billion. The major medical treatment for these losses are transplantation of tissues and organs; however, these transplantations are severely limited by donor shortages (1). The shortages of replacement tissue and organs have generated a substantial research effort on the development of alternative sources for transplantations. Improved cultivation of cells and tissues so that the processes of organ failure and organogenesis are better understood may yield better approaches to either avoid pathological organ failure or allow the creation of new replacement tissues and organs for transplantations. While molecular biology has provided critical insight into the pathological processes that cause organ failure, the capacity for renewal of organ function is limited not only by deficits in the knowledge of the molecular biology, but also in the ability to culture cells from normal adult organs and to make them function appropriately outside of the host from which they arose. A major advancement would be the ability to achieve three-dimensional cell propagation resulting in differentiated and functional tissue. Unfortunately, most present day culture systems provide only occasional evidence of cellular diversification and differentiation. Conventional culture techniques attach cells to a planar substratum that produces a two-dimensional monolayer over the surface. While this configuration may optimize mass transfer of oxygen and nutrients to cells, it only supports inadequate two-dimensional intercellular interactions. Recent data from three-dimensional cultures of cells in gels or spheroids have shown that important aspects of normal and neoplastic differentiation are controlled by three-dimensional interactions including the ability to form tubules and to induce resistance to chemotherapy by cancer cells. However, these three-dimensional systems are limited in the number of cells cultured whereas recovery of cells and factors from gel systems is cumbersome. Thus, there is a need for growing batch cultures in three-dimensions in aqueous media.

NASA's bioreactor program was instituted to investigate the problem of cell maintenance and viability in the space environment to support biological experiments. This research found that the stresses to which cells were subjected should be minimized in order to culture cells with a low rate of morbidity. The NASA biotechnology research group applied a clinostat, a cell maintenance system in which the container was rotated, to minimize the shear forces. This method of cell suspension creates shear stresses for small cell aggregates that are significantly smaller than those in conventional, stirred bioreactors. Mammalian cells cultured in this low shear environment aggregate and grow into relatively large masses, and the cultured cells display differentiation markers similar to those found in mammalian tissues (2). In addition, cells have sustained concentrations that are 2 - 4 times denser than in conventional bioreactors. The advantage of this system is that tissue-like cell densities are suspended in a well-mixed aqueous medium that facilitates nutrient transfer, dispersion of wastes, and also makes possible the isolation of potentially novel factors. In addition, co-cultivation of cancer cells with normal cells produces tissues that mimic the structure of the cancer as it appears in the intact host. Similarly, bone and cartilage cultures have recreated the appearance and much of the strength of the normal tissue. These results suggest that the propagation of cells in a culture system are dependent on a low shear stress environment, spatial co-location of participating cell populations, and matrix materials that promote the morphology of the desired tissue.

Ground-based research studies have demonstrated that both normal and neoplastic cells recreate many of the characteristics in the NASA bioreactor that they display in tissues. Proximal renal tubule cells that normally have rich apically oriented microvilli with intercellular clefts in the kidney do not form any of these structures in two-dimensional monolayer culture. However, when normal proximal renal tubule cells are cultured in three-dimensions in the bioreactor, both the microvilli and the intercellular clefts appear, and the cells form small tubules. Similar results

in recreating normal structures have occurred in bone and cartilage cultures. Cultivation of small intestinal enterocytes has not been possible to date in conventional culture systems, but human small bowel intestinal cells have been cultivated in the bioreactor successfully for over 2 months (3). In other studies with malignant cells investigators have been able to recreate the morphologic appearance of metastases to liver by human colon carcinoma (4), to bone by human prostate carcinoma cells, or to various organs by other carcinomas. These studies have generally involved co-cultivation of the malignant cell with the normal cells that form the scaffolding of these organs and have recreated the three-dimensional shape of the cancerous tissue. This is important because when the morphology is recreated, the function is more likely also to be rejuvenated. This is born out by related studies by Kerbel and co-workers (5,6) who have recently found that three-dimensional cultures of many different types of malignant cells are resistant to chemotherapy that normally kills these tumor cells in two-dimensional monolayer culture. Thus, the ground-based studies with malignant cells that recreate the morphological appearance and behavior of metastases in an animal or man may provide a good test for the development of new therapeutic agents as well as improving our understanding of how prior chemotherapy might be made more effective.

Ground-based studies with the bioreactor have also achieved two other milestones. First, it has been essentially impossible to date to routinely establish primary breast or prostate cancers in culture. However, investigators at the University of South Florida have achieved an impressive 80% success rate in establishing cultures of primary breast cancers. In addition, investigators at the University of Texas M.D. Anderson Cancer Center have previously shown that when human colon cancer cells form masses within the bioreactor, they produce factors that stimulate the growth and differentiation of normal colon cells when the factors are placed back in the colon of an animal (7). Conventional cultures of these same colon cancer cells did not produce the same stimulatory activity. Thus, ground-based studies have shown that the bioreactor has achieved successful growth of fastidious malignant cells and that it permits the production of factors that are not detectable in conventional bioreactor cultures.

Objectives and Description of Participation

The program has three major goals concerning mammalian tissue culture: 1) to accelerate the development of a three-dimensional tissue culturing system using rotating-wall bioreactors, 2) to define and characterize mammalian cells and tissues that benefit from a low shear environment, and 3) to use the microgravity environment of space as necessary to surmount the obstacles to the propagation of complex tissues.

- Ground-based Proposals
  Ground-based experimental and theoretical research proposals submitted under this announcement should address the above tissue culturing goals. Potential areas of research for investigators are as follows:

  a) Investigate the effect of reduced levels of mechanical and hydrodynamic shear, spatial co-location of participating cell populations, and the role of mass transport on cellular propagation and tissue assembly in rotating wall bioreactor systems.
  b) Research the effects of culture media (growth factors, etc.), cellular metabolism, and waste accumulation to facilitate the propagation of differentiated, functioning tissues in space and ground-based bioreactors.
  c) Assess the value of low shear and spatial co-location culturing by establishing functional tissue to do morphological analysis using rotating wall vessels. This research must be able to quantitatively measure determinable parameters such as tissue mass, tissue differentiation or diversification markers, tissue function, or production of biologically active materials.
  d) Research to support the development of technologies (biosensors for pH, glucose, and oxygen levels, etc.), techniques, and maintenance strategies for three-dimensional tissue culture to allow long-term automation and improve the tissue culturing process.

e) Research that offers new tissue culturing methods and strategies that produce three-dimensional tissue propagation.

f) Investigate the physical environment produced in the bioreactor as a model for understanding the cellular response to microgravity. This research may lead to a more expeditious use of the microgravity environment in tissue engineering and cell culture.

- Flight Proposals
  Proposals in this category would involve tissue systems that have demonstrated enhanced growth and differentiation in ground-based rotating vessel research. NASA is carrying out preliminary development work on flight hardware capable of supporting mammalian tissue culture studies (see Appendix B for instrument descriptions).

  Investigations proposing flight experiments should be sufficiently mature from a scientific and technical standpoint to define a flight investigation and proceed to a review of their concept within two years of their initial funding. A clear need for reduced gravity should be described either theoretically or experimentally. Several possible levels of participation are envisioned for flight investigations: (1) proposers may offer to design and develop instruments under contract with NASA, (2) proposers may offer to provide instrument components to planned or existing hardware such as the thermal enclosure flight hardware, (3) proposers may offer to develop simple hardware that can be used within the capabilities of the glovebox, or (4) proposers may offer research to be performed in NASA developed or international instruments with the proposer providing scientific guidance to the development effort (see Appendix B for instrument descriptions).

D. PROTEIN CRYSTAL GROWTH

Introduction

NASA has demonstrated, through crystallization experiments conducted on the Space Shuttle, that reducing one crystallization parameter, gravity, can have a significant effect on the quality of certain protein crystals. In order to build on these results, NASA is developing a research program to study protein crystallization and provide a framework for understanding microgravity protein crystallization results, optimize growth conditions for protein crystals formed in the microgravity environment of space, and provide a more rational approach to the growth of macromolecular crystals. NASA-sponsored ground-based research over the past several years has produced significant advances in our knowledge of the physical chemistry of protein crystallization and has contributed to evolving technologies for monitoring, controlling, and automating crystal growth. Under this research announcement, the protein crystal growth program will expand its ground-based and flight research efforts.

Structural determination of biological macromolecules is essential to progress in the biological sciences and pharmaceutical industry. The determination of accurate macromolecular structures is necessary for establishing the molecular mechanisms of biological reactions for rational drug design (in which a molecule is designed to bind to a specific target protein) and for the design of proteins and nucleic acids with new activities and functions. During the past decade the methods of protein crystallography have been made faster and more accurate through the use of improved data collection methodologies and more powerful computers. Almost all proteins and nucleic acids can be made in sufficiently large quantities for crystallographic analysis using the methodologies of cloning genes or by direct chemical synthesis. This means that any biological macromolecule for which there is a gene sequence can, in principle, become a subject for study by protein crystallography if the growth of high quality protein crystals is possible. Currently, the growth of such crystals is a limiting step to progress on important structural problems.

Determination of crystal structure by protein crystallography requires well-ordered, single crystals whose minimum dimension is approximately 0.2 to 0.4 mm. The accuracy of the resulting coordinates derived from determining a crystal structure is directly related to the resolution to which the crystals diffract and, therefore, to the quality of the crystal. Structures determined at higher resolutions when properly refined have smaller errors in atomic coordinates compared to

those determined at lower resolutions. Proteins whose structures are refined to 2 Å or better and have coordinate errors of about 0.2 Å require very high quality crystals. These high quality crystals produce the increase in diffraction data necessary to get to higher resolution.

In unit gravity, macromolecular crystallization is affected by convection in the solution surrounding the growing crystals and sedimentation of these crystals. Protein crystals form more slowly than inorganic compounds and may be even more susceptible to convection and sedimentation effects. Improvements in the size and order of protein crystals grown in the microgravity environment of space are possible because it is conjectured that crystal growth in a purely diffusive transport regime limits local supersaturation by forming depletion zones around the growing crystals (5). This allows a more ordered and regulated delivery of molecules to the surfaces of the crystals, it serves as a filter that prevents the incorporation of disordered aggregates and larger impurities, and discourages secondary nucleation near growing crystals. In addition, microgravity's elimination of sedimentation decreases contacts between crystals that might otherwise affect their morphology and degree of quality. As a result, the resolution of the diffraction pattern from protein crystals formed in microgravity are often higher than the resolution achieved for the same protein crystallized on Earth. Thus, the microgravity environment affords an opportunity to study how crystals form and achieve better packing, and this may, in turn, lead to solution of more complex structures. Unfortunately, there is currently no agreed upon physical basis to explain the results from the Shuttle protein crystallization experiments.

NASA first flew protein crystal growth experiments in 1985 using a device operated by an astronaut to test the adaptation of the hanging drop technique to the space environment. This device was succeeded by the more automated vapor diffusion apparatus (VDA) which was housed in a thermal enclosure and flown in the Shuttle middeck. Despite a number of technical difficulties, the project has made progress, some of which is documented in the references given below. These include, in some cases, the growth of crystals to sizes and degrees of quality that surpass samples grown in conventional laboratories and the formation of crystals in useful habits which had not been previously observed in ground-based experiments.

Three recent Shuttle missions, IML-1, IML-2, and USML-1, produced very encouraging results regarding macromolecular crystallization in microgravity. These are summarized in papers by DeLucas et al. (1,2,3), Day and McPherson (4), McPherson (5) and Koszelak et al. (6). Orthorhombic crystals of satellite tobacco mosaic virus (STMV) grown by liquid:liquid diffusion in microgravity were more than 15 times the volume of similar crystals grown on Earth (4). These crystals provided diffraction data to 1.8 Å resolution (an improvement from 2.3 Å resolution and represented an increase of useful diffraction data of nearly 50%). This in turn allowed investigators to determine the structure to the highest resolution yet achieved for any virus. In experiments on IML-2, liquid-liquid diffusion was again used to probe cubic crystals of STMV more than 30 times the volume of comparable Earth-grown crystals, and improved crystalline samples of the protein canavalin as well (6). Data from these latter crystals allowed extension of the resolution of the canavalin structure from 2.7 Å to 2.2 Å. In addition to these enhancements of diffraction quality, a number of intriguing morphological changes in several crystals, clearly attributable to the microgravity environment, were also observed (4-6).

Evidence of the effects of the microgravity environment on macromolecular crystallization obtained from flight investigations, coupled with new data on the mechanisms and influences that govern such growth are converging to some hypotheses that can be evaluated experimentally. Currently, NASA is in the process of developing a new generation of flight hardware that will allow more macromolecular samples to be flown, automated control of the crystallization process, and will provide means for the direct observation of the crystal growth phenomenon as it occurs in space. This will allow the quantification of essential thermodynamic and kinetic parameters, delineation of relevant mechanisms, and the identification of optimal macromolecular samples.

Objectives and Description of Participation

The program has the following goals concerning protein crystal growth: 1) to form an integrated effort using the space environment for the advancement in understanding of the fundamental factors influencing macromolecular nucleation and growth, 2) to elucidate which of these factors

provide the observed benefits in diffraction performance when protein crystal nucleation and growth is conducted in microgravity, 3) to contribute to the structural knowledge of biological macromolecules and macromolecular assemblages (viruses, etc.) through the growth of crystals suitable for x-ray diffraction analysis by utilizing the space environment, 4) to determine the roles protein crystal nucleation and growth in microgravity may play in extending crystallographic analyses to more complex and challenging systems, such as glycoproteins, lipoproteins, and integral membrane proteins, 5) to develop technologies and quantitative methodologies that will improve the protein crystallization process on Earth as well as in space.

- Guest Investigator Program
  Researchers who are not seeking financial support but who are solely interested in opportunities to use the space environment to improve the quality of a particular protein crystal should not submit a proposal to this announcement, but should contact Dr. Daniel Carter of the Marshal Space Flight Center at (205) 544-5492 to find out about the Guest Investigator Program.

- Ground-based Proposals
  Under this announcement, NASA is soliciting ground-based proposals for scientific research focusing on understanding the fundamental processes that create and order protein crystals; NASA's eventual goals are to reproducibly grow protein crystals of improved quality and allow the growth of previously uncrystallized proteins. This announcement is also soliciting research that will lead to technological developments that will improve protein crystal growth techniques.

- Flight Proposals
  Investigations proposing flight experiments should be sufficiently mature from a scientific and technical standpoint to define a flight investigation and proceed to a review of their concept within two years of their initial funding. A clear need for reduced gravity should be described either theoretically or experimentally. Several possible levels of participation are envisioned for flight investigations: (1) proposers may offer to design and develop instruments under contract with NASA, (2) proposers may offer to provide instrument components to planned or existing hardware such as the thermal enclosure flight hardware, (3) proposers may offer to develop simple hardware that can be used within the capabilities of the glovebox, or (4) proposers may offer research to be performed in NASA developed or international instruments with the proposer providing scientific guidance to the development effort (see Appendix B for instrument descriptions).

E. FUNDAMENTALS OF BIOTECHNOLOGY

Introduction

Expansion of biological technologies is required for the United States to retain a competitive advantage in biotechnology. This expansion requires an understanding of the fundamental processes on which these technologies are based. NASA is currently defining a program in fundamentals of biotechnology which will study those processes which are affected by buoyancy driven convection and sedimentation, and that can be gainfully studied using the low-gravity (diffusion controlled transport) environment of space. Gravity's effect on these processes can be virtually eliminated in space; thus allowing space-based experiments, coupled with ground-based experimental and theoretical research, to provide insights into biotechnological processes. NASA's goal is to exploit the unique microgravity environment of space to advance the understanding of basic phenomenon, and use the information gained through space experimentation on a wide range of biotechnology applications.

The Fundamentals of Biotechnology area of NASA's Biotechnology Program has historically been composed of research on electrophoresis, isoelectric focusing and phase partitioning. Significant progress has been made in understanding the physics of these separation technologies. For example, knowledge gained from these experiments regarding the role of transport in separation processes is now applied directly to the design of commercial electrophoresis units. Space research has allowed the study of separation processes without the effects of buoyant flow and the sedimentation of suspended material caused by gravity. NASA-sponsored model samples showed the importance of electrohydrodynamics, (EHD), as a

dominant fluid disturbance in wide-gap electrophoresis chambers. A series of isoelectric focusing experiments conducted in free fluids or gels on two Shuttle missions clearly showed EHD destroyed the desired high resolution focusing. This research is currently investigating the coupling of fluid flows and the applied electric fields, thus providing insight into phenomena such as electrohydrodynamic instabilities. Phase partitioning is limited on Earth due to sedimentation of both cells and phase droplets, so several small experiments were done on the Shuttle to explore the benefits of this technique in space.

The focus of this announcement is to solicit new concepts in fundamentals of biotechnology which may mature to flight research. Potential research areas include 1) molecular aggregation, 2) diffusion studies on macromolecules, 3) separation and purification studies, 4) the behavior of electrically-driven flows as related to biological separations, 5) capillary and surface phenomena as applied uniquely to biological systems, and 6) membrane transport phenomena affected by diffusion controlled conditions in microgravity. Proposals for theoretical research in this area which are connected to, or have an enabling role for investigations which seek to ultimately use the space environment, will be considered for support through this announcement.

Objectives and Description of Participation

This announcement is intended primarily to solicit experimental investigations in Fundamentals of Biotechnology which will establish the scientific foundations for future flight experiment development. Proposals for flight experiments which are mature and could proceed to flight using simple hardware designed to work inside the glovebox or using existing hardware with little modification are also solicited under this announcement.

- Ground-based Proposals
  Experimental and theoretical research proposals are requested that define and characterize biotechnological phenomena and processes for which microgravity represents an enabling environment. Ground-based proposals submitted in this area should be focused on understanding biotechnological phenomena which require the low gravity environment to test a scientific hypothesis or which can be advantageously studied in the space environment. The program has as its near-term objective the development of a knowledge base sufficient to assess the scientific value of fundamental experiments in biotechnology under low gravity conditions, where diffusion controlled conditions dominate and sedimentation is essentially eliminated. The primary intent of this announcement is to select investigations which will form a coherent effort in understanding the scientific utility of microgravity for fundamental research and to begin to define simple middeck flight experiments.

- Flight Proposals
  Investigations proposing flight experiments should be sufficiently mature from a scientific and technical standpoint to define a flight investigation and proceed to a review of their concept within two years of their initial funding. A clear need for reduced gravity should be described either theoretically or experimentally. Several possible levels of participation are envisioned for flight investigations: (1) proposers may offer to design and develop instruments under contract with NASA, (2) proposers may offer to provide instrument components to planned or existing hardware such as the thermal enclosure flight hardware, (3) proposers may offer to develop simple hardware that can be used within the capabilities of the glovebox, or (4) proposers may offer research to be performed in NASA developed or international instruments with the proposer providing scientific guidance to the development effort (see Appendix B for instrument descriptions).

III. EXPERIMENTAL APPARATUS AND FLIGHT OPPORTUNITIES

A. EXPERIMENTAL APPARATUS

Several flight instruments have been developed by NASA in order to address the objectives of the biotechnology disciplines described in the preceding section. **Appendix B provides brief capability descriptions of the flight hardware and ground-based reduced-gravity testing facilities.**

B. FLIGHT OPPORTUNITIES

Missions available for this program may include several Shuttle missions, missions aboard the Russian Mir space station, and missions on the International Space Station.

Space Shuttle flights are usually of 7-10 days duration, although some flights longer than 10 days are planned. The Russian Mir space station and International Space Station will be ideal for long duration experiments. Residual acceleration levels of the order of 10^{-4}g are available in a Space Shuttle orbiter. The acceleration environment aboard the Space Station should be substantially better during certain time periods. A space acceleration measurement system is expected to be available for the measurement and recording of actual accelerations.

Downlink channels enable investigators to monitor their instrument status and science data streams in real time. Uplink channels enable investigators to adjust their experimental parameters in near real time. Flight experiment protocols should also consider the additional benefits that could be derived from skilled crew interaction with experiments available during many of these flight opportunities.

C. EXPERIMENT DEFINITION AND FLIGHT ASSIGNMENT PROCESS

Ground-based research is usually necessary to clearly define flight experiment objectives. Successful proposals for flight opportunities will be supported for a ground-based definition phase before review for flight assignment. The amount of support (technical, scientific, and budgetary) and the length of the definition period (usually from 6 months to 2 years) will depend on the specific investigator needs and the availability of resources from NASA. However, in preparing their budget plan for this research announcement, all respondents should estimate their annual costs for four years.

1. Near-Term Flight Opportunities. Successful proposals for use of existing instruments will be funded for a period of advanced definition work, after which time the investigator will generate a detailed SRD. The SRD, a detailed experiment description outlining the specific experiment parameters and conditions, as well as the background and justification for flight, must be prepared jointly by a NASA-appointed Project Scientist and the Principal Investigator and submitted for peer review. This formal review by both science and engineering panels will determine if space flight is required to meet the science objectives and if instrument capabilities can be provided to meet the science requirements. Following approval by the review panels, subject to program resources, continuation support will be awarded and the hardware will be modified to meet the science requirements. NASA does not guarantee that any experiment selected for definition will advance to flight experiment status. Investigations with unresolved science or engineering issues at the review of the SRD may be placed in ground-based status with support of limited duration (normally from one to three years), and asked to submit a proposal to a subsequent solicitation for further support.

2. Future Flight Opportunities. Successful proposals for the development of new apparatus will be funded for a period of definition. The length of the definition period will be based on the experiment requirements, but will generally be from 6 to 24 months. At the end of the experiment definition phase, the investigator will generate a detailed SRD. Following successful peer review of the SRD by science and engineering panels, the experiment will proceed into flight development and be considered for flight. As with

opportunities for existing instruments, NASA does not guarantee that any experiment selected for definition will advance to flight development status, and the possibility exists that investigations may be placed in ground-based status, with continuing support from NASA for a limited period.

3. Ground-Based Definition Opportunities. Promising proposals for experimental research which are not mature enough to allow development of an SRD after two years of definition, and proposals for development of theory in areas of current or potential microgravity experiments, may be selected for support in the MSAD Research and Analysis (R&A) Program. R&A studies are funded for periods of up to four years. A new proposal to a future announcement is required in order to be selected for a flight opportunity or to continue R&A studies if appropriate.

IV. PROPOSAL SUBMISSION INFORMATION

This section gives the requirements for submission of proposals in response to this announcement. The research proposal submitted under this announcement consists of a Principal Investigator who is responsible for all research activities and one or more Co-Investigators. Proposers must address all the relevant selection criteria in their proposal as described in Section VI and must format their proposal as described in this section. Additional general information for submission of proposals in response to NASA Research Announcements may be found in Appendix C.

A. LETTER OF INTENT

Organizations planning to submit a proposal in response to this NRA should notify NASA of their intent to propose by electronically sending a Letter of Intent (LOI) via the web to the following address:

https://peer1.idi.usra.edu/mail/biotech/letter_of_intent.html

Letters of Intent may be submitted via e-mail to the following address: loi@hq.nasa.gov
If electronic means are not available, you may mail Letters of Intent to the address given for proposal submission in the following section.

The Letter of Intent, which should not exceed two pages in length, must be typewritten in English and must include the following information:

- The potential Principal Investigator (PI), position, organization, address, telephone, fax, and e-mail address.
- A list of potential Co-Investigators (Co-I's), positions, and organizations.
- General scientific/technical objectives of the research.
- The equipment of interest listed in this NRA, if appropriate.

The Letter of Intent should be received at NASA Headquarters no later than July 19, 1996. The Letter of Intent is being requested for informational and planning purposes only, and is not binding on the signatories. The Letter of Intent allows NASA to better match expertise in the composition of peer review panels with the response from this solicitation. Investigators may also request more detail on the capabilities of the specific equipment that might be utilized to accomplish their scientific objectives.

B. PROPOSAL

The proposal should not exceed 20 pages in length, exclusive of appendices and supplementary material, and should be typed on 8-1/2 x 11 inch paper with a 10- or 12-point font. Extensive appendices and ring-bound proposals are discouraged. Reprints and preprints of relevant work will be forwarded to the reviewers if submitted as attachments to the proposal.

In preparation of proposals, the standard forms and certifications at the back of this research announcement should be used. Proposers should prepare cost estimates by year for a period not greater than four years in preparing budget plans in response to this research announcement.

Fifteen copies of the proposal must be received at NASA Headquarters by August 27, 1996, 4:30 PM EDT to assure full consideration. Treatment of late proposals is described in Appendix C. Send proposals to the following address:

NASA c/o Information Dynamics Inc.
Subject: NASA Research Proposal (NRA-96-OLMSA-03)
300 D Street, S.W.
Washington, D.C. 20024
Telephone number for delivery services: (202) 479-2609

Proposals submitted in response to this Announcement must contain at least the following information in the format shown below:

- Title Page
- Table of Contents
- Executive Summary (replaces abstract) (1-2 pages)
- Research Project Description
  - Statement of the hypothesis, objective, and value of this research
  - Review of relevant research
  - Justification for new or further microgravity research
  - Description of Experimental or Analytical Method
  - Data Analysis
  - References
- Appendices
  - Proposed Costs (see Appendix C, Section 7-I and below)
  - Current and Pending Support
  - Management Approach
  - Complete vitae for the PI and all Co-investigators
  - Facilities and Equipment (see Appendix C, Section 7-h)
  - Signed Certifications (see below)
- **3.5 inch computer diskette containing electronic copy of principal investigator's name, address, complete project title, and executive summary**

The title page must clearly identify the research announcement to which the proposal is responding, title of the proposed research, principal investigator, institution, address and telephone number, total proposed cost, proposed duration, and must contain all signatories.

The executive summary should succinctly convey, in broad terms, what it is the proposer wants to do, how the proposer plans to do it, why it is important, and how it meets the requirements for microgravity relevance. The executive summary replaces the proposal abstract.

Each proposal requesting financial support should include signed Certifications Regarding Lobbying; Debarment, Suspension and other Responsibility Matters; and Drug-Free Workplace Requirements. Copies of these certifications may be found at the end of this document.

Proposal Cost Detail Desired. Sufficient proposal cost detail and supporting information will facilitate a speedy evaluation and award. Dollar amounts proposed with no explanation (e.g., Equipment: $58,000, or Labor: $10,000) may cause delays in evaluation or award. The proposed costing information should be sufficiently detailed to allow the Government to identify cost elements for evaluation purposes. Generally, the Government will evaluate cost as to reasonableness, allowability, and allocability. Enclose explanatory information, as needed. Each category should be explained. Offerors should exercise prudent judgement as the amount of detail necessary varies with the complexity of the proposal.

V. ADDITIONAL GUIDELINES FOR INTERNATIONAL PARTICIPATION

NASA accepts proposals from all countries, although this program does not financially support Principal Investigators in countries other than the U.S. Proposals from non-U.S. entities should not include a cost plan. **Non-U.S. proposals and U.S. proposals which include non-U.S. participation, must be endorsed by the appropriate government agency in the country from which the non-U.S. participant is proposing.** Such endorsement should indicate:

1. The proposal merits careful consideration by NASA.
2. If the proposal is selected, sufficient funds will be made available to undertake the activity as proposed.

Proposals, along with the requested number of copies (15) and Letter of Endorsement, must be forwarded to NASA in time to arrive before the deadline established for this NRA.

The Endorsement Letter, along with one copy of the proposal, must be sent to:

Ms. Ruth Rosario
Space Flight Division
Office of External Relations
Code IH
National Aeronautics and Space Administration
Washington, DC 20546-0001
USA

All proposals must be typewritten in English. All non-U.S. proposals will undergo the same evaluation and selection process as those originating in the U.S.

Successful and unsuccessful proposers will be notified by mail directly by the NASA program office coordinating the NRA. Copies of these letters will be sent to the sponsoring government agency. Should a non-U.S. proposal or U.S. proposal with non-U.S. participation be selected, NASA's Office of External Relations will arrange with the non-U.S. sponsoring agency for the proposed participation on a no-exchange-of funds basis, in which NASA and the appropriate government agency will each bear the cost of discharging its respective responsibilities. Depending on the nature and extent of the proposed cooperation, these arrangements may entail: (1) A letter of notification by NASA, (2) An exchange of letters between NASA and the sponsoring government agency, and (3) An agreement or memorandum of understanding between NASA and the sponsoring government agency.

VI. EVALUATION AND SELECTION

A. EVALUATION PROCESS. The evaluation process for this NRA will begin with a scientific and technical peer review of the submitted proposals. NASA will conduct an engineering review of the potential hardware requirements for proposals that include flight experiments. The programmatic objectives of this NRA, as discussed in the introduction to this Appendix, will be applied by NASA to enhance program breadth, balance, and diversity. NASA will also evaluate the cost of the proposal. Upon completion of deliberations, offerors will be notified regarding proposal selection or rejection. Offerors whose proposals are declined will have the opportunity of a verbal debriefing with a NASA representative regarding the reasons for this decision. Additional information on the evaluation and selection process is given in Appendix C.

B. EVALUATION FACTORS. The following section replaces Section 13 of Appendix C.

The principal elements considered in the evaluation of proposals solicited by this NRA are: relevance to NASA's objectives, intrinsic merit, and cost. Of these, intrinsic merit has the greatest weight, followed by relevance to NASA's objectives, which has slightly lesser weight. Both of these elements have greater weight than cost. Evaluation of the intrinsic merit of the proposal includes consideration of the following factors, in descending order of importance:

1. Overall scientific or technical merit, including evidence of unique or innovative methods, approaches, or concepts, and the potential for new discoveries or understanding;
2. Qualifications, capabilities, and experience of the proposed principal investigator, team leader, or key personnel who are critical in achieving the proposal objectives;
3. Institutional resources and experience that are critical in achieving the proposal objectives;
4. Overall standing among similar proposals available for evaluation and/or evaluation against the known state-of-the-art.

Evaluation of the cost of a proposed effort includes consideration of the realism and reasonableness of the proposed cost, and the relationship of the proposed cost to available funds.

C. SELECTION CATEGORIES AND PERIOD OF SUPPORT

Proposals selected for support through this NRA will be selected as either ground-based investigations or flight definition investigations. Investigators offered support in the ground-based program will be required to submit a new proposal for competitive renewal after no more than four years of support. Investigators offered flight definition status are expected to begin preparing detailed experiment requirements and concepts for flight development shortly after selection in cooperation with the assigned representative from a NASA center. The selected investigations will be required to comply with NASA policies, including the return of all appropriate information for inclusion in the archives during the performance of and at the completion of the contract or grant.

VII. NRA FUNDING

The total amount of funding for this program is subject to the annual NASA budget cycle. The Government's obligation to make awards is contingent upon the availability of appropriated funds from which payment for award purposes can be made and the receipt of proposals which the Government determines are acceptable for an award under this NRA.

For the purposes of budget planning, we have assumed that the Microgravity Science and Applications Division will fund four flight experiment definition proposals. These definition-phase proposals will be funded on an average of $175,000 per year. Approximately 20 ground-based study proposals will be funded, at an average of $125,000 per year, for up to 4 years. The initial fiscal year (FY) 1997 funding for all proposals will be adjusted, if required, to reflect partial fiscal year efforts. The proposed budget for ground-based studies should include researcher's salary,

travel to science and NASA meetings (for a flight investigation, roughly eight meetings per year with NASA should be anticipated, though travel activity will vary over the development of the experiment), other expenses (publication costs, computing or workstation costs), burdens, and overhead. During subsequent years, NRA's similar to this NRA will be issued, and funds are planned to be available for additional investigations.

VIII. BIBLIOGRAPHY

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The *Microgravity Science and Applications Program Tasks and Bibliography for FY 1995* (NASA Technical Memorandum 4735, March 1996) may provide useful information to proposers (see page *vi* for address to obtain a copy).

HARDWARE AND FACILITY DESCRIPTIONS

MICROGRAVITY BIOTECHNOLOGY: RESEARCH AND FLIGHT EXPERIMENT OPPORTUNITIES

NASA's Microgravity Science and Applications Division is currently pursuing a program for the development of payloads capable of accommodating multiple users. This program is expected to meet the science requirements of microgravity investigations and to support the development of technologies for microgravity biotechnology research. In the interest of minimizing project cost and complexity, NASA encourages the use of existing hardware whenever consistent with experiment requirements.

The equipment described is either planned for development or has been developed by NASA for flight on the Shuttle and other space platforms. International equipment described here may be offered for flight on a cooperative basis with agencies from various countries. The specific availability of certain flight hardware is subject to coordination with the Center for Macromolecular Crystallography and approval from the OSAT Space Processing Division prior to the finalization of arrangements for flight opportunities. The availability of the hardware described in this section is contingent upon the availability of funds, flight manifest opportunities, and, for international hardware, cooperative agreements between NASA and the appropriate foreign space agency.

I. CURRENT FLIGHT HARDWARE

The experimental hardware described in this section is available with or without modification contingent upon the availability and allocation of resources.

I. Middeck Glovebox (MGBX) (NASA/MSFC)

The Middeck Glovebox is multiuser and multidiscipline facility that provides an enclosed working space for experiment manipulation and observation. Glovebox Investigations which have flown include: protein crystal growth, fluid physics, combustion, and materials science experiments.

The MGBX occupies two standard lockers in the Space Shuttle middeck. The MGBX door opening to insert or retrieve investigation hardware is 20.3 cm by 19.4 cm, with a working volume of 35 liters. Forced air cooling can withdraw a maximum of 60 W of investigation generated heat. Up to 60 W of 24, ± 12, and 5 VDC power is available for experimenter apparatus. The MGBX can be used in various modes of pressure and air circulation. The working area can serve as a sealed environment that is isolated from the crew cabin atmosphere, as a constantly recirculating atmosphere that is maintained at a pressure slightly lower that the middeck ambient, or as a working area open to the middeck. Multipurpose filters exist to remove particles, liquids, and reaction gasses from the recirculated air.

Due to limitations of the Space Shuttle middeck, there is no standard data or video downlink. There is the possibility of some near real-time video downlink (from the Shuttle Camcorder), but this will be decided on a mission-by-mission basis. Four video recorders provide data storage, with digital data stored in the audio channels; an additional connector records eight channels of data to the Interface frame data recorder. An adjustable light switch, video port plugs, a backlight panel, a halogen flashlight, redlight filters, and cutout window covers provide illumination.

II. THERMAL ENCLOSURES

Use of the Single-locker Thermal Enclosure System (STES) or the Thermal Enclosure System (TES) is encouraged for investigations requiring experiment temperature control. The Gaseous Nitrogen Dewar/Freezer (GN2 Dewar) can be used for samples that need to be frozen. Because the STES, TES, and GN2 Dewar are frequently manifested in the middeck of the Shuttle Orbiter, the equipment can be installed shortly before a launch. Current timetables provide late access at approximately 24 hours before launch and early removal at three-to-eight hours after Shuttle landing.

Ideally, equipment built to be accommodated in the TES or STES should be fully automated: experiments should be initiated and terminated automatically. However, some crew time may be available for tending of experiments (e.g., deployment of protein samples) on some flights. The proposer should recognize that crew time and communication channels are subject to mission priorities that place experiment management behind crew health, safety concerns, and accomplishment of the primary mission first.

A. Single Locker Thermal Enclosure System (STES)

The STES is the size of a single middeck locker and provides a controlled temperature environment within plus or minus 0.5° C of a set point in the range from 1 to 40° C; the set point must be within 24° C of ambient temperature. The STES time/temperature profile is programmable within the thermal capability of the hardware. Internal STES heat is transferred primarily by conduction. The STES has nine sensors which are placed at various locations to record temperature history and to provide temperature control. Temperature data is available post-mission. A payload assembly, consisting of an STES and an experiment apparatus, must meet interface, operational, and safety requirements of the vehicle or space platform used. Section III below provides information on selected experiment apparatus accommodation. A small amount of power is available for use by an experiment apparatus; use of this resource may impact the temperature control capability of the unit. Experiment duration, available crew time, and air-to-ground communication capability for STES payloads is mission dependent. Periodic monitoring of STES operation is required. The STES door can be opened easily to accommodate experiment operations.

B. Thermal Enclosure System (TES)

The TES is the size of two vertically adjacent middeck lockers and provides a controlled temperature environment within plus or minus 0.2° C of a set point in the range from 1 to 40° C; the set point must be within 24° C of ambient temperature. The TES time/temperature profile is programmable within the thermal capability of the hardware. Internal TES heat is transferred primarily by convection. The TES has nine sensors which are placed at various locations to record temperature history and to provide temperature control. Temperature data is available post-mission. A payload assembly, consisting of a TES and an experiment apparatus, must meet interface, operational, and safety requirements of the vehicle or space platform used. Section III below provides information on experiment apparatus accommodation. A small amount of power is available for use by an experiment apparatus; use of this resource may impact the temperature control capability of the unit. Experiment duration, available crew time, and air-to-ground communication capability for TES payloads is mission dependent. Periodic monitoring of TES operation is required. The TES door is not normally removed for experiment operations: mechanical and electrical/electronic functions are accomplished by use of "feed throughs" in the TES door. An experiment-unique TES door may be proposed.

C. Gaseous Nitrogen Dewar (GN2 Dewar)

The GN2 Dewar is a device used to transport and maintain samples at cryogenic temperatures. Units can be flown in a standard Shuttle middeck locker and are available by agreement with the Johnson Space Center. These existing units are capable of maintaining a cryogenic temperature for six-to-13 days. Passive cooling is provided by absorbed liquid nitrogen which slowly

evaporates from the dewar. Depletion rate for the nitrogen is specific to the unit used, and the units cannot be recharged on orbit. Samples may be launched in a GN2 Dewar and then allowed to thaw in a microgravity environment. Sample holders or experiment devices may be designed to be housed in a GN2 Dewar, but must meet certain size and design requirements.

III. PROTEIN CRYSTAL GROWTH HARDWARE

A. Protein Crystallization Apparatus for Microgravity (PCAM)

The PCAM is a protein crystal growth device that has been developed to provide a large number of protein crystallization experiments in a single middeck locker flight. Six cylindrical PCAM units can be mounted in an STES unit. Each cylindrical PCAM contains nine crystallization plates, each having seven sample chambers, for a total of 63 chambers per cylinder. Thus, the total number of samples that can be flown in an STES is 378. The crystallization plates are modified "sitting drop" vapor diffusion devices. In the center of each chamber is a pedestal with a depression on its top which can contain up to 40 microliters of pre-mixed protein sample solution and precipitant solution. The pedestal is surrounded by a toroidal reservoir of absorbent material capable of containing one milliliter of precipitant solution. The protein solution is isolated from the reservoir prior to activation and after deactivation. Activation occurs simultaneously for all chambers in a cylinder, as does deactivation.

B. Vapor Diffusion Apparatus (VDA)

The VDA and the advanced VDA (or VDA-2) are protein crystal growth devices based around a syringe assembly design for mixing protein solutions and precipitant solutions on orbit. VDA trays are designed to fit inside the STES units. An STES can accommodate three VDA trays and four VDA-2 trays. Each VDA tray consists of 20 double-barreled syringes, and each VDA-2 tray has 20 triple-barreled syringes. One barrel of each syringe can be loaded with up to 30 microliters of protein solution, and a second barrel with up to 30 microliters of precipitant solution. Absorbent reservoir material containing approximately one milliliter of precipitant solution surrounds the drop in each chamber. The experiment is initiated by deployment of the solutions onto the tips or the syringe assemblies to form drops. Mixing of drops is effected by moving the droplet solutions into and out of the syringes. In the case of the VDA-2, the third barrel is used for mixing and this results in improved mixing. The experiment is deactivated by moving the drops back into the syringes. Prior to drop deployment and after deactivation the solutions in the syringes are sealed with plugs that press against the syringe tips.

C. Advanced Crystal Observation System (ACOS)

The ACOS is a protein crystal growth diagnostic tool now under development for the PCG flight program. ACOS experiment apparatus can be accommodated in an STES. The ACOS consists of two 20-chamber VDA-2 trays, described above, which are viewed by a translating video camera. The purpose of the ACOS experiment is to observe the growth dynamics of crystals in growth solutions.

D. Commercial Vapor Diffusion Apparatus (CVDA)

This experiment flight hardware was developed to allow commercial customers to grow protein crystals in a configuration that is similar to typical laboratory hardware using the vapor diffusion method. The CVDA provides a greatly improved thermal environment, sample capacity, and operational scenario over previous VDA flight hardware. The CVDA increases the sample capacity to 128 growth chambers within one thermal enclosure. The internal configuration of the growth chambers was designed to mimic a Limbro box. The protein and precipitating agent are separated in individual syringe barrels prior to activation.

E. Protein Crystallization Facility (PCF)

This equipment is used for batch processing of proteins that show a temperature dependence on solubility. The PCF sample bottles range from 50 ml to 500 ml, accommodating four sample bottles in one thermal enclosure. This equipment has flown several times, performing with a high degree of predictability. Sample bottles are made from polysulfone with a Teflon coated aluminum lid.

F. Protein Crystallization Facility - Light Scattering Temperature (PCF-LST)

The PCF-LST grows crystals using the same temperature induced growth process as the PCF. The PCF-LST incorporates a laser light scattering device that detects nucleation and displays the corresponding detector voltage level on a Macintosh Powerbook. This display allows a crew member to identify when nucleation has occurred in the sample and to adjust the temperature profile accordingly to control the growth period. This experiment hardware accommodates two sample bottles up to 50 milliliters in size, in one thermal enclosure. In addition, approximately one standard middeck locker of stowage is required for support equipment.

G. Protein Crystallization Facility-Variable Gradient (PCF-VG)

This equipment is used to allow customers to process small amounts of protein using the temperature induced crystal growth process. Sample sizes for the PCF-VG include 1 ml and 5 ml. By varying thermal path configurations internal to the thermal enclosure used, investigators can obtain several temperature profiles for different samples. By allowing customers to screen a large number of conditions on a single flight, users are able to investigate a variety of growth parameters.

IV. TISSUE CULTURE SYSTEMS

The tissue culture systems provide the technological capability for addressing the potential of microgravity tissue and cell culturing. These rotating culture vessels offer increased levels of tissue culturing capability and automation, thus allowing the investigator to culture many types of cells under low mechanical stress culture conditions. These culture vessels rotate the suspended cells and tissue and the vessel wall about a horizontal axis creating a low fluid shear environment. The vessels include features that allow addition of nutrients, removal of metabolic waste products, respiratory gas exchange, temperature control, and sample removal. The vessels have been used successfully to culture suspension and anchorage-dependent mammalian cells.

1. Slow Turning Lateral Vessel (STLV)

The STLV is a nonperfused, horizontally rotating bioreactor consisting of a fixed volume vessel (50 or 100 ml). The vessel is connected to a variable-rate motor and mounted on a fixed base. The STLV is autoclavable. The vessel has several separate sample ports for adding media or reagents and removing samples. The STLV has been optimized for to culture anchorage-dependent cells on microcarrier systems.

2. High Aspect Ratio Vessel (HARV)

The HARV is a nonperfused, horizontally rotating bioreactor consisting of a fixed volume vessel (10 or 50 ml) with a large radius and a short length. The vessel is connected to a variable-rate motor and mounted on a fixed base. The HARV is autoclavable. The vessel has several separate sample ports for adding media or reagents and removing of samples. The HARV has been optimized to culture suspension cells and anchorage-dependent cells with or without microcarriers.

3. The Rotating Wall Perfused Vessel (RWPV)

The RWPV is a perfused, horizontally rotating bioreactor consisting of a fixed volume vessel (250 or 500 ml), a silicone membrane oxygenator, a pH sensor, sample ports, and a pump for infusing or recycling fresh medium. The RWPV is sterilized with ethylene oxide in a specially designed apparatus. The vessel is secured to a support base and connected to two variable-rate motors that independently control the rotation of the vessel's outer wall and the hollow inner centerline spin filter. Rotation rates for the vessel's outer wall and spin filter can be varied in order to create different levels of fluid shear and turbulence. Samples are withdrawn through sample ports; the vessel's outer wall can be stopped temporarily during sampling. Fresh or recycled media can be perfused into the vessel at rates sufficient to support nutrient delivery, metabolic gas exchange, and waste-product removal. A version of the RWPV has been used to transition cell cultures to microgravity.

4. The Biotechnology Specimen Temperature Controller (BSTC)

The BSTC is flight equipment capable of transporting and maintaining biological and cell culture samples in a controlled temperature. The BSTC is a self-contained unit that can maintain a variety of specimen volumes up to 50 ml in as many as 4 independent temperature controlled blocks ranging from 7 to 37° C. The device can maintain target temperatures in this range during launch, mission and reentry. The temperature profiles for the blocks can be maintained independently. Each block measures approximately 2.7 cm x 5.2 cm x 1.4 cm. Energy dependent cell functions can be investigated in microgravity by controlling the incubation temperature.

V. INTERNATIONAL BIOTECHNOLOGY EQUIPMENT

A. Cryostat (Deutsche Luft-und Raumfahrt, DARA, Germany)

The Cryostat is a device developed for conducting experiments on the crystallization of proteins. The Cryostat has successfully flown on previous Shuttle missions and is available for future flights as a middeck payload. The equipment allows for a protein solution and a salt solution to be mixed through a buffer solution on orbit. When a shutter separating the protein and the salt solution from the buffer is slowly removed under microgravity conditions, the species diffuse from opposite sides into the buffer, where crystals of the protein can thus be formed. In the cryostat, two containers are accommodated, each allowing the processing of four such samples. Additionally, a 24 sample modified sitting drop container is available for use. U.S. investigators could plan on choosing up to half of the samples to be processed.

The thermal conditions during processing can be controlled $\pm$ 0.5° C between -10° C and +20° C by means of Peltier heating and cooling elements. The sample temperature can be held constant at 20° C during storage periods prior to and after processing. Temperature data is recorded during processing. The samples are returned for analysis along with data on the performance of the hardware. Late access to the facility for loading samples can be as late as two days prior to launch. Early removal of the samples from the vehicle can occur within several hours after landing.

B. Automated Protein Crystallization Facility (APCF) (European Space Agency, ESA)

The APCF is a multiuser facility dedicated to the growth of protein crystals. The APCF has successfully flown on previous Shuttle missions as a middeck payload and provides a wide range of experimental conditions. The following methods for crystallization can be employed: liquid/liquid interface diffusion, dialysis, or vapor diffusion.

An APCF occupies one Shuttle middeck locker space. A unit can contain up to 48 samples. Experimenters can choose different volumes for the solutions, typically 4-470 µL. Temperature control within the APCF is $\pm$ 0.3°C for any preselected temperature between 4°C and 20°C. Ten crystal growth reactors can be monitored by B/W CCD video cameras and data from laser light

scattering by micron size particles is available. The facility can be monitored for reactor status and temperature data. The process is fully automated, requiring crew intervention only to start (power on and initialize crystallization process) and to end (terminate process and power off) the experiment. The samples are returned with the Shuttle for analysis along with digitized video and imaging and hardware performance data. Late access to the facility for loading samples can be as late as two days prior to launch. Early removal of the samples from the vehicle can occur within several hours after landing.

C. Free Flow Electrophoresis Unit (FFEU)
(National Space Development Agency of Japan, NASDA)

The FFEU is a multi-user Spacelab facility developed for the study of electrophoresis in space. The FFEU is a continuous flow electrophoresis unit which flew previously on Spacelab-J. Electrophoresis occurs in a sealed chamber containing the FFEU fluid components (buffer pumps, fluid pumps, etc.). Sixty (60) separation ports are available. Sample materials are stored in interchangeable cassettes and are installed in the FFEU on orbit. Each cassette hold 0.6 ml of sample material. An adjustable electric field, maximums of 100mA and 100 V/cm, can be applied across the flow, causing the differently charged components to deflect into separate streams (fractions) which are monitored by a photometer using an ultra-violet light source. The maximum flow rate is 25 ml/min. One of three buffer solutions can be selected by the crew. The separation chamber can be cooled below 5° C. Ultraviolet absorbency monitoring of separation chambers is available. Samples are returned to earth for analysis. Late access to the facility for loading samples can be as late as one to two days prior to launch. Early removal of the samples from the vehicle can occur within several hours after landing.

D. Applied Research on Separation Methods using Space Electrophoresis (French Acronym: RAMSES) (French National Center for Space Studies, CNES)

RAMSES is a multi-user Spacelab facility designed to support basic and applied research on electrophoresis in space. It is a continuous flow zone electrophoresis unit. The sample material to be purified is continuously injected into a flowing buffer solution and carried across the separation chamber. The sample capacity is 10-20 ml. An adjustable electric field, 100 mA for 0-150V, 50 mA for 150-300V, can be applied across the flow, causing the differently charged components to deflect into separate streams (fractions) which are monitored by a photometer using an ultraviolet light source. When the photometer detects a significant amount of biological material in the output flow, each stream is individually collected in a total of 40 output ports. Otherwise the flow is diverted to a waste tank. Separation parameters – flow rates, electric field strengths, and buffer fluid temperature – can be altered to study a wide range of conditions. Separation experiments can also be monitored and photographed through a transparent window in the instrument front panel. A cross-illumination source provides a plane light sheet across the separation chamber that produces an image of the sample flow in cross section when viewed from the correct angle. Samples and cross-illumination photographs are returned to Earth for analysis. Other sensor data can be returned to Earth via the Spacelab data downlink. Late access to the facility for loading samples can be as late as one to two days prior to launch. Early removal of the samples from the vehicle can occur within several hours after landing.

VI. OTHER BIOTECHNOLOGY FLIGHT HARDWARE

A. Commercial Generic Bioprocessing Apparatus (CGBA)

The CGBA payload consists of a combination of temperature controlled locker replacement modules and fluid containment/mixing devices. It is compatible with Shuttle middeck, Spacehab, Spacelab and Mir interface requirements. Preparation of the CGBA payload allows samples to be loaded off-site and shipped to KSC for final integration, if so desired. Late access handover (L-24 hours) minimizes the time required between loading and launch for viable samples. Established protocol provides the opportunity to perform synchronized ground controls in flight-like hardware. Clinorotation in flight hardware is also available. The payload has flown on 8 STS missions since 1992 returning over 2000 cumulative biological and material samples at a better than 99% success ratio. Experiments supported by CGBA have included: micro-organism growth,

eucaryotic cell response, virus capsid formation, crystal growth, collagen and fibrin polymerization, and mammalian tissue development. The individual components of CGBA are described below.

Fluid Processing Apparatus (FPA)

An FPA is essentially a "microgravity test tube". The first level of sample containment consists of a glass barrel (1.35 cm id x 11.7 cm) with movable rubber septa used to confine the fluids in separate chambers within the barrel. All components contacting the sample material are fully autoclavable allowing sterility to be maintained. The design provides initial isolation of 2 or 3 fluids and allows subsequent, on-orbit mixing. Fluid mixing is achieved as the fluid and septa are pushed forward until the fluid reaches a molded bypass in the glass barrel and flows around the forward septum into the adjacent chamber. The standard configuration provides a total liquid volume of 6.5 ml loaded as follows:1.5 ml fixative / 1.5 ml initiator / 3.5 ml precursor. A sealed, Lexan sheath with a plunger handle encompasses the glass barrel providing an activation mechanism and a second level of containment. A positive pressure integrity test to 5 psid is performed on this preflight. Visual observation of samples in an FPA is possible and in-flight video or still photographs can be obtained.

Many variations of fluid volumes and configurations are possible. Several examples of modified FPAs include:

1. Gas Exchange-FPA (GE-FPA): The GE-FPA has a gas permeable endcap and an O-ring Lexan insert is used in place of the distal rubber septum, thus allowing gas exchange between sample and entire GAP volume.

2. Expanded Volume-FPA (EV-FPA): Provides up to 10 ml into 1 ml mixing capability.

Group Activation Pack (GAP)

The GAP provides a third level of fluid containment composed of Lexan and aluminum. It allows simultaneous activation of 8 FPAs through attachment of a manual crank handle to a drive mechanism. (Used in GBA-INC or can be stowed in an ambient locker). A positive pressure integrity test to 5 psi is also performed on the GAPs preflight.

Auto-GAP

Same as the GAP, but activated automatically by an external DC motor drive rather than a manual crank. (Used in GBA-ICM).

GBA-INC

The GBA-INC is a middeck locker equivalent providing stowage for 9 GAPs(72 FPAs) at 37° C. Uniform temperature control is achieved using top and bottom strip heaters thermally coupled to the GAP aluminum endcaps. Optical density (565 nm) monitoring capability of 8 FPAs concurrently allows high resolution reaction rate data to be collected real-time.

GBA-ICM

GBA-ICM is a middeck locker equivalent which provides temperature controlled stowage for 8 GAPs (64 FPAs) adjustable between 4° C and 37° C. Thermoelectric modules are used to transfer heat to/from active water loops distributed around all 6 sides to virtually eliminate thermal gradients. An accelerometer-based system is used to detect launch, thus allowing the GAPs to begin initiating experiments immediately upon entering orbit. Additionally, automatic GAP determination can be programmed to occur at any time during the mission, including just prior to reentry based on preplanned (or updated) end of mission time. Combined, these two capabilities allow an early-as-possible experiment initiation and a late-as-possible termination; periods when crew availability for manual tasks is at a minimum. GBA-ICM also provides control versatility in light of launch delays, and can take advantage of mission duration extensions.

B. ADvanced SEPerations (ADSEP).

ADSEP is a fully-automated, processing unit that fits into a middeck or Spacehab locker. It is capable of separating living cells and cellular organelles using aqueous two-phase partitioning. The flight hardware contains three independently controlled processing modules, which can be programmed for totally automated operation or controlled via telemetry. Processing temperature can be independently controlled and regulated between 4-40° C in each of the three processing modules. Biological samples are loaded into a liquid-tight cassette assembly, which allows the cassettes to be installed and removed from the ADSEP modules on orbit. Processing consists of mixing with a programmable electromagnetic stirring system, and indexing the sample storage plates countercurrently. Each sample can be processed through up to 22 stages, employing a wide range of mixing, separation, and indexing parameters. In addition to separating cells, ADSEP has been employed for other fluids experiments where mechanical agitation, electromagnetic fields, and/or transfer of liquids from one well to the next is desired.

C. Materials Dispersion Apparatus (MDA) Minilab

The MDA is an automated laboratory which conducts approximately 100 fluid experiments within a brick-sized volume. Experiments which have been successfully conducted with this hardware include protein and other crystal growth, microencapsulation, thin film membrane formation, live cell culture studies, collagen formation, seed germination, and fluid science research. The heart of the MDA consists of a pair of blocks containing dozens of small test-tube like volumes of 20 to 500 uL each. Once in microgravity, the blocks are moved and the fluids which were separated are brought together to mix by either liquid-liquid diffusion, vapor diffusion, turbulent mixing, or wetting, depending upon the experiment design. As an option, the two liquids can be separated at a later time, or a third can be mixed in, such as a fixative for a cell culture experiment.

The MDA Minilab has to date successfully processed hundreds of biotechnology and other samples on the Shuttle. Four of the MDA Minilabs can be placed within a temperature-controlled middeck locker, for a total of up to 400 samples per locker. The MDA has flown on six Shuttle missions, along with six sounding rocket flights and the KC-135 low-g aircraft.

II. GROUND-BASED FACILITIES

Investigators often need to conduct reduced gravity experiments in ground-based facilities during the experiment definition and technology development phases. The NASA ground-based reduced gravity research facilities that support the MSAD combustion program include two drop towers at the Lewis Research Center (LeRC), a DC-9 and KC-135 aircraft.

A. 2.2-SECOND DROP TOWER

The 2.2-Second Drop Tower at LeRC provides 2.2 second of low-gravity test time for experiment packages consisting of up to 125 kilograms of hardware. The experiment package is enclosed in a drag shield and a gravitational acceleration of less than 10^{-5}g is obtained during the fall since the experiment package falls freely within the drag shield. At the end of a drop, the drag shield and the enclosed experiment are decelerated in a 2.2-meter deep sand pit by the deceleration spikes. The peak deceleration rate can be as high as 70g's. Eight to twelve tests can be performed in one day. Data from experiments are acquired by high speed motion picture cameras with rates up to 1,000 frames per second and by onboard data acquisition systems used to record data supplied by thermocouples, pressure transducers, and flow meters.

B. 5.18-SECOND ZERO-GRAVITY FACILITY

The 5.18-second Zero-Gravity at LeRC has a 132-meter free fall distance in a drop chamber which is evacuated by a series of pumpdown procedures to a final pressure of 1 Pa. Experiments with hardware weighing of up to 450 kilograms are mounted in a one-meter diameter by 3.4-meter high drop bus. Gravitational acceleration of less than 10^{-5}g is obtained. At the end of the drop, the bus is decelerated in a 6.1-meter deep container filled with small

pellets of expanded polystyrene. The deceleration rate is typically 60g (for 20 millisec). Visual data is acquired through the use of high-speed motion picture cameras. Also, other data such as pressures, temperatures, and accelerations are either recorded onboard with various data acquisition systems or are transmitted to a control room by a telemetry system capable of transmitting 18 channels of continuous data. Due to the complexity of drop chamber operations and time required for pump-down of the drop chamber, typically only one test is performed per day.

C. DC-9 and KC-135 AIRCRAFT

The aircraft can provide up to 40 periods of low-gravity for 25-second intervals each during one flight. The aircraft accommodates a variety of experiments and is often used to refine space flight experiment equipment and techniques and to train crew members in experiment procedures, thus giving investigators and crew members valuable experience working in a weightless environment. The aircraft obtain a low-gravity environment by flying a parabolic trajectory. Gravity levels twice those of normal gravity occur during the initial and final portions of the trajectory, while the brief pushover at the top of the parabola produces less than one percent of Earth's gravity (10^{-2}g). Several experiments, include a combination of attached and free-floated hardware (which can provide effective gravity levels of 10^{-3} for periods up to 10 seconds) can be integrated in a single flight. Both 28-volt DC and 100-volt AC power are available. Instrumentation and data collection capabilities must be contained in the experiment packages.

III. COMPUTATIONAL SUPPORT AND DATA MANAGEMENT

NASA provides an advanced computational environment incorporating supercomputers, high performance mass storage, and software. NASA also provides an on-line, multidisciplinary directory of space science data sets of interest to the NASA-sponsored research community. NASA has chartered the NASA Science Internet (NSI) to provide transparent wide-area network connectivity to NASA researchers, computational resources, and data, worldwide. Each of these facilities and resources should be considered by an investigator to determine which are required for conducting biotechnology research. Investigators should include any requirements for theses resources in their proposal.

INSTRUCTIONS FOR RESPONDING TO NASA RESEARCH ANNOUNCEMENTS (JUNE 1995)

1. Foreword

a. These instructions apply to NASA Research Announcements. The "NASA Research Announcement (NRA)" permits competitive selection of research projects in accordance with statute while preserving the traditional concepts and understandings associated with NASA sponsorship of research.

b. These instructions are Appendix I to 1870.203 of the NASA Federal Acquisition Regulation Supplement.

2. Policy

a. Proposals received in response to an NRA will be used only for evaluation purposes. NASA does not allow a proposal, the contents of which are not available without restriction from another source, or any unique ideas submitted in response to an NRA to be used as the basis of a solicitation or in negotiation with other organizations, nor is a pre-award synopsis published for individual proposals.

b. A solicited proposal that results in a NASA award becomes part of the record of that transaction and may be available to the public on specific request; however, information or material that NASA and the awardee mutually agree to be of a privileged nature will be held in confidence to the extent permitted by law, including the Freedom of Information Act.

3. Purpose

These instructions supplement documents identified as "NASA Research Announcements." The NRAs contain programmatic information and certain requirements which apply only to proposals prepared in response to that particular announcement. These instructions contain the general proposal preparation information which applies to responses to all NRAs.

4. Relationship to Award

a. A contract, grant, cooperative agreement, or other agreement may be used to accomplish an effort funded in response to an NRA. NASA will determine the appropriate instrument.

b. Grants are generally used to fund basic research in educational and nonprofit institutions, while research in other private sector organizations is accomplished under contract. Contracts resulting from NRAs are subject to the Federal Acquisition Regulation and the NASA FAR Supplement (NHB 5100.4). Any resultant grants or cooperative agreements will be awarded and administered in accordance with the NASA Grant and Cooperative Agreement Handbook (NHB 5800.1).

5. Conformance to Guidance

a. NASA does not have mandatory forms or formats for preparation of responses to NRAs; however, it is requested that proposals conform to the guidelines in these instructions. NASA may accept proposals without discussion; hence, proposals should initially be as complete as possible and be submitted on the proposers' most favorable terms.

b. In order to be considered responsive, a submission must, at a minimum, present a specific project within the areas delineated by the NRA; contain sufficient technical and cost information to permit a meaningful evaluation; be signed by an official authorized to legally bind the submitting organization; not merely offer to perform standard services or to just provide

computer facilities or services; and not significantly duplicate a more specific current or pending NASA solicitation.

6. NRA-Specific Items

a. Several proposal submission items appear in the NRA itself. These include: the unique NRA identifier; when to submit proposals; where to send proposals; number of copies required; and sources for more information. Items included in these instructions may be supplemented by the NRA.

7. Proposal Contents

a. The following information is needed in all proposals in order to permit consideration in an objective manner. NRAs will generally specify topics for which additional information or greater detail is desirable. Each proposal copy shall contain all submitted material, including a copy of the transmittal letter if it contains substantive information.

b. **Transmittal Letter or Prefatory Material.** (1) The legal name and address of the organization and specific division or campus identification if part of a larger organization;

(2) A brief, scientifically valid project title intelligible to a scientifically literate reader and suitable for use in the public press;

(3) Type of organization: e.g., profit, nonprofit, educational, small business, minority, women-owned, etc.;

(4) Name and telephone number of the principal investigator and business personnel who may be contacted during evaluation or negotiation;

(5) Identification of other organizations that are currently evaluating a proposal for the same efforts;

(6) Identification of the NRA, by number and title, to which the proposal is responding;

(7) Dollar amount requested , desired starting date, and duration of project;

(8) Date of submission; and

(9) Signature of a responsible official or authorized representative of the organization, or any other person authorized to legally bind the organization (unless the signature appears on the proposal itself).

c. **Restriction on Use and Disclosure of Proposal Information**

Information contained in proposals is used for evaluation purposes only. Offerors or quoters should, in order to maximize protection of trade secrets or other information that is confidential or privileged, place the following notice on the title page of the proposal and specify the information subject to the notice by inserting appropriate identification, such as page numbers, in the notice. In any event, information contained in proposals will be protected to the extent permitted by law, but NASA assumes no liability for use and disclosure of information not made subject to the notice.

NOTICE

Restriction on Use and Disclosure of Proposal Information. The information (data) contained in [insert page numbers or other identification] of this proposal constitutes a trade secret and/or information that is commercial or financial and confidential or privileged. It is furnished to the Government in confidence with the understanding that it will not, without permission of the offeror, be used or disclosed other than for evaluation purposes; provided, however, that in the event a contract (or other agreement) is awarded on the basis of this proposal the Government shall have the right to use and disclose this information (data) to the extent provided in the contract (or other agreement). This restriction does not limit the Government's right to use or disclose this information (data) if obtained from another source without restriction.

d. **Abstract.** Include a concise (200-300 word if not otherwise specified in the NRA) abstract describing the objective and the method of approach.

e. **Project Description**. (1) The main body of the proposal shall be a detailed statement of the work to be undertaken and should include objectives and expected significance; relation to the present state of knowledge; and relation to previous work done on the project and to related work in progress elsewhere. The statement should outline the plan of work, including the broad design of experiments to be undertaken and a description of experimental methods and procedures. The project description should address the evaluation factors in these instructions and any specific factors in the NRA. Any substantial collaboration with individuals not referred to in the budget or use of consultants should be described. Subcontracting significant portions of a research project is discouraged.

(2) When it is expected that the effort will require more than one year for completion, the proposal should cover the complete project to the extent that it can be reasonably anticipated. Principal emphasis should, of course, be on the first year of work, and the description should distinguish clearly between the first year's work and work planned for subsequent years.

f. **Management Approach**. For large or complex efforts involving interactions among numerous individuals or other organizations, plans for distribution of responsibilities and arrangements for ensuring a coordinated effort should be described. Intensive working relations with NASA field centers that are not logical inclusions elsewhere in the proposal should be described.

g. **Personnel**. The principal investigator is responsible for supervision of the work and participates in the conduct of the research regardless of whether or not compensated under the award. A short biographical sketch of the principal investigator, a list of principal publications and any exceptional qualifications should be included. Omit social security number and other personal items which do not merit consideration in evaluation of the proposal. Give similar biographical information on other senior professional personnel who will be directly associated with the project. Give the names and titles of any other scientists and technical personnel associated substantially with the project in an advisory capacity. Universities should list the approximate number of students or other assistants, together with information as to their level of academic attainment. Any special industry- university cooperative arrangements should be described.

h. **Facilities and Equipment**. (1) Describe available facilities and major items of equipment especially adapted or suited to the proposed project, and any additional major equipment that will be required. Identify any Government-owned facilities, industrial plant equipment, or special tooling that are proposed for use.

(2) Before requesting a major item of capital equipment, the proposer should determine if sharing or loan of equipment already within the organization is a feasible alternative. Where such arrangements cannot be made, the proposal should so state. The need for items that typically can be used for research and non-research purposes should be explained.

I. **Proposed Costs**. (1) Proposals should contain cost and technical parts in one volume: do not use separate "confidential" salary pages. As applicable, include separate cost estimates for salaries and wages; fringe benefits; equipment; expendable materials and supplies; services; domestic and foreign travel; ADP expenses; publication or page charges; consultants; subcontracts; other miscellaneous identifiable direct costs; and indirect costs. List salaries and wages in appropriate organizational categories (e.g., principal investigator, other scientific and engineering professionals, graduate students, research assistants, and technicians and other non-professional personnel). Estimate all manpower data in terms of man-months or fractions of full-time.

(2) Explanatory notes should accompany the cost proposal to provide identification and estimated cost of major capital equipment items to be acquired; purpose and estimated number and lengths of trips planned; basis for indirect cost computation (including date of most recent negotiation and cognizant agency); and clarification of other items in the cost proposal that are not self- evident. List estimated expenses as yearly requirements by major work phases. (Standard Form 1411 may be used).

(3) Allowable costs are governed by FAR Part 31 and the NASA FAR Supplement Part 18-31 (and OMB Circulars A-21 for educational institutions and A-122 for nonprofit organizations).

j. **Security**. Proposals should not contain security classified material. If the research requires access to or may generate security classified information, the submitter will be required to comply with Government security regulations.

k. **Current Support**. For other current projects being conducted by the principal investigator, provide title of project, sponsoring agency, and ending date.

l. **Special Matters**. (1)Include any required statements of environmental impact of the research, human subject or animal care provisions, conflict of interest, or on such other topics as may be required by the nature of the effort and current statutes, executive orders, or other current Government-wide guidelines.

(2) Proposers should include a brief description of the organization, its facilities, and previous work experience in the field of the proposal. Identify the cognizant Government audit agency, inspection agency, and administrative contracting officer, when applicable.

8. Renewal Proposals

a. Renewal proposals for existing awards will be considered in the same manner as proposals for new endeavors. A renewal proposal should not repeat all of the information that was in the original proposal. The renewal proposal should refer to its predecessor, update the parts that are no longer current, and indicate what elements of the research are expected to be covered during the period for which support is desired. A description of any significant findings since the most recent progress report should be included. The renewal proposal should treat, in reasonable detail, the plans for the next period, contain a cost estimate, and otherwise adhere to these instructions.

b. NASA may renew an effort either through amendment of an existing contract or by a new award.

9. Length

Unless otherwise specified in the NRA, effort should be made to keep proposals as brief as possible, concentrating on substantive material. Few proposals need exceed 15-20 pages. Necessary detailed information, such as reprints, should be included as attachments. A complete set of attachments is necessary for each copy of the proposal. As proposals are not returned, avoid use of "one-of-a-kind" attachments: their availability may be mentioned in the proposal.

10. Joint Proposals

a. Where multiple organizations are involved, the proposal may be submitted by only one of them. It should clearly describe the role to be played by the other organizations and indicate the legal and managerial arrangements contemplated. In other instances, simultaneous submission of related proposals from each organization might be appropriate, in which case parallel awards would be made.

b. Where a project of a cooperative nature with NASA is contemplated, describe the contributions expected from any participating NASA investigator and agency facilities or equipment which may be required. The proposal must be confined only to that which the proposing organization can commit itself. "Joint" proposals which specify the internal arrangements NASA will actually make are not acceptable as a means of establishing an agency commitment.

11. Late Proposals

A proposal or modification received after the date or dates specified in an NRA may be considered if the selecting official deems it to offer NASA a significant technical advantage or cost reduction.

12. Withdrawal

Proposals may be withdrawn by the proposer at any time. Offerors are requested to notify NASA if the proposal is funded by another organization or of other changed circumstances which dictate termination of evaluation.

13. Evaluation Factors

a. Unless otherwise specified in the NRA, the principal elements (of approximately equal weight) considered in evaluating a proposal are its relevance to NASA's objectives, intrinsic merit, and cost.

b. Evaluation of a proposal's relevance to NASA's objectives includes the consideration of the potential contribution of the effort to NASA's mission.

c. Evaluation of its intrinsic merit includes the consideration of the following factors, none of which is more important than any other:

(1) Overall scientific or technical merit of the proposal or unique and innovative methods, approaches, or concepts demonstrated by the proposal.

(2) Offeror's capabilities, related experience, facilities, techniques, or unique combinations of these which are integral factors for achieving the proposal objectives.

(3) The qualifications, capabilities, and experience of the proposed principal investigator, team leader, or key personnel critical in achieving the proposal objectives.

(4) Overall standing among similar proposals and/or evaluation against the state-of-the-art.

d. Evaluation of the cost of a proposed effort includes the realism and reasonableness of the proposed cost and the relationship of the proposed cost and available funds.

14. Evaluation Techniques

Selection decisions will be made following peer and/or scientific review of the proposals. Several evaluation techniques are regularly used within NASA. In all cases proposals are subject to scientific review by discipline specialists in the area of the proposal. Some proposals are reviewed entirely in-house, others are evaluated by a combination of in-house and selected external reviewers, while yet others are subject to the full external peer review technique (with due regard for conflict-of- interest and protection of proposal information), such as by mail or through assembled panels. The final decisions are made by a NASA selecting official. A proposal which is scientifically and programmatically meritorious, but not selected for award during its initial review, may be included in subsequent reviews unless the proposer requests otherwise.

15. Selection for Award

a. When a proposal is not selected for award, and the proposer has indicated that the proposal is not to be held over for subsequent reviews, the proposer will be notified. NASA will explain generally why the proposal was not selected. Proposers desiring additional information may contact the selecting official who will arrange a debriefing.

b. When a proposal is selected for award, negotiation and award will be handled by the procurement office in the funding installation. The proposal is used as the basis for negotiation. The contracting officer may request certain business data and may forward a model contract and other information which will be of use during the contract negotiation.

16. Cancellation of NRA

NASA reserves the right to make no awards under this NRA and to cancel this NRA. NASA assumes no liability for canceling the NRA or for anyone's failure to receive actual notice of cancellation. Cancellation may be followed by issuance and synopsis of a revised NRA, since amendment of an NRA is normally not permitted.

NASA RESEARCH ANNOUNCEMENT (NRA) SCHEDULE

MICROGRAVITY BIOTECHNOLOGY:
RESEARCH AND FLIGHT EXPERIMENT OPPORTUNITIES

All proposals submitted in response to this Announcement are due on the date and at the address given below by the close of business (4:30 PM EDT). NASA reserves the right to consider proposals received after this deadline if such action is judged to be in the interest of the U.S. Government. A complete schedule of the review of the proposals is given below:

NRA Release Date: ..... May 24, 1996

Letter of Intent Due: ..... July 19, 1996

Proposal Due: ..... August 27, 1996

Submit Proposal to:

NASA c/o Information Dynamics Inc.
Subject: NASA Research Proposal (NRA-96-OLMSA-03)
300 D Street, S.W., Suite 801
Washington, D.C. 20024
Telephone number for delivery services: (202) 479-2609

Final Selections: ..... April 1997

Funding commences: ..... June 1997
(dependent upon procurement process)

FORM A

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
OFFICE OF LIFE & MICROGRAVITY SCIENCES & APPLICATIONS
MICROGRAVITY SCIENCE AND APPLICATIONS DIVISION

SOLICITED PROPOSAL APPLICATION
PLEASE FOLLOW INSTRUCTIONS CAREFULLY

LEAVE BLANK
NUMBER
REVIEW GROUP
DATE RECEIVED

1. COMPLETE TITLE OF PROJECT

2. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR *(First, middle, and last name; degrees; position title)*

3. COMPLETE MAILING ADDRESS
Department
Institution
Street
City, state, zip code

4. TELEPHONE NUMBER *(area code, number, extension)*
FAX NUMBER
E-MAIL ADDRESS

5. CONGRESSIONAL DISTRICT

6. SOCIAL SECURITY #

7. IS THIS PROPOSAL ⁄ NEW ⁄ RENEWAL ⁄ REVISED

8. HAS THIS PROPOSAL (OR SIMILAR REQUEST) BEEN SUBMITTED TO NASA OR ANY OTHER AGENCY?
⁄ No ⁄ Yes IF YES, SPECIFY AGENCY AND YEAR SUBMITTED:

9. HUMAN SUBJECTS

9a. ⁄ No ⁄ Yes

9b. EXEMPTION # OR IRB APPROVAL DATE_____

9c. Assurance of Compliance #_____

10. VERTEBRATE ANIMALS

10a. ⁄ No ⁄ Yes

10b. ACUC Approval Date_____

10c. PHS Animal Welfare Assurance #_____

11. DATES OF ENTIRE PROPOSED PROJECT PERIOD	12. COSTS REQUESTED FOR FIRST 12-MONTH BUDGET PERIOD		13. COSTS REQUESTED FOR ENTIRE PROPOSED PROJECT PERIOD	
	12a. Direct Costs	12b. Total Costs	13a. Direct Costs	13b. Total Costs
From:	$	$	$	$
Through:				

14. APPLICANT ORGANIZATION *(Organization Name)*

15. TYPE OF ORGANIZATION
⁄ Non Profit ⁄ For Profit *(General)* ⁄ For Profit *(Small Business)* ⁄ Public, Specify: ⁄ Federal ⁄ State ⁄ Local

16. ORGANIZATION OFFICIAL TO BE NOTIFIED IF AN AWARD IS MADE *(Name, title, address and telephone number)*

17. OFFICIAL SIGNING FOR APPLICANTORGANIZATION *(Name, title, and telephone number)*

18. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE:
I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application. Willful provision of false information is a criminal offense (U.S. Code, Title 18, Section 1001).

SIGNATURE OF PERSON NAMED IN 2
(In ink "Per" signature not acceptable.)
DATE

19. CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true and complete to the best of my knowledge, and accept the obligation to comply with NASA terms and conditions if a grant is awarded as the result of this application. A willfully false certification is a criminal offense (U.S. Code, Title 18, Section 1001).

SIGNATURE OF PERSON NAMED IN 17
(In ink "Per" signature not acceptable.)
DATE

FORM B

PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: _____

DETAILED BUDGET FOR 12-MONTH BUDGET PERIOD DIRECT COSTS ONLY		FROM	THROUGH		
Duplicate this form for each year of grant support requested		DOLLAR AMOUNT REQUESTS *(Omit cents)*			
PERSONNEL *(Applicant Organization Only)*		**EFFORT ON PROJECT**	**SALARY**	**FRINGE BENEFITS**	**TOTALS**
NAME	**ROLE IN PROJECT**				
	Principal Investigator				
	SUBTOTALS →				
CONSULTANT COSTS					
EQUIPMENT *(Itemize, use additional sheet if needed)*					
SUPPLIES *(Itemize by category, use additional sheet if needed)*					
TRAVEL	DOMESTIC				
	FOREIGN				
OTHER EXPENSES *(Itemize by category, use additional sheet if needed)*					

TOTAL DIRECT COSTS FOR FIRST 12-MONTH BUDGET PERIOD *(Item 12a, Form A)*	**$**
INDIRECT COSTS FOR FIRST 12-MONTH BUDGET PERIOD	**$**
TOTAL COSTS FOR FIRST 12-MONTH BUDGET PERIOD *(Item 12b, Form A)*	**$**

FORM C

PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: _____

BUDGET FOR ENTIRE PROJECT PERIOD DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	1st BUDGET PERIOD	ADDITIONAL YEARS OF SUPPORT REQUESTED		
		2nd	3rd	4th
PERSONNEL (Salary and Fringe Benefits) (Applicant organization only)				
CONSULTANT COSTS				
EQUIPMENT				
SUPPLIES				
TRAVEL – DOMESTIC				
TRAVEL – FOREIGN				
OTHER EXPENSES				
TOTAL DIRECT COSTS FOR EACH BUDGET PERIOD	**$**	**$**	**$**	**$**
TOTAL INDIRECT COSTS FOR EACH BUDGET PERIOD	**$**	**$**	**$**	**$**
TOTAL DIRECT + INDIRECT COSTS FOR EACH PERIOD	**$**	**$**	**$**	**$**

TOTAL DIRECT + INDIRECT COSTS FOR ENTIRE PROJECT	**$**

JUSTIFICATION FOR UNUSUAL EXPENSES (Detail Justification in Cost Section of Proposal)

FORM D

CERTIFICATION REGARDING DRUG-FREE WORKPLACE REQUIREMENTS

This certification is required by the regulations implementing the Drug-Free Workplace Act of 1988, 34 CFR Part 85, Subpar F. The regulations, published in the January 31, 1989 Federal Register, require certification by grantees, prior to award, tha they will maintain a drug-free workplace. The certification set out below is a material representation of fact upon which reliance will be placed when the agency determines to award the grant. False certification or violation of the certification shall be grounds for suspension of payments, suspension or termination of grants, or government-wide suspension or debarment (see 34 CFR Part 85, Sections 85.615 and 85.620).

I. GRANTEES OTHER THAN INDIVIDUALS

A. The grantee certifies that it will provide a drug-free workplace by:

(a) Publishing a statement notifying employees that the unlawful manufacture, distribution, dispensing, possession or use of a controlled substance is prohibited in the grantee's workplace and specifying the actions that will be taken against employees for violation of such prohibition;

(b) Establishing a drug-free awareness program to inform employees about --

(1) The dangers of drug abuse in the workplace;

(2) The grantees policy of maintaining a drug-free workplace;

(3) Any available drug counseling, rehabilitation, and employee assistance programs; and

(4) The penalties that may be imposed upon employees for drug abuse violations occurring in the workplace;

(c) Making it a requirement that each employee to be engaged in the performance of the grant be given a copy of the statement required by paragraph (a);

(d) Notifying the employee in the statement required by paragraph (a) that, as a condition of employment under the grant, the employee will --

(1) Abide by the terms of the statement; and

(2) Notify the employer of any criminal drug statute conviction for a violation occurring in the workplace no later than five days after such conviction;

(e) Notifying the agency within ten days after receiving notice under subparagraph (d) (2) from an employee or otherwise receiving actual notice of such conviction;

(f) Taking one of the following actions, within 30 days of receiving notice under subparagraph (d) (2), with respect to any employee who is so convicted --

(1) Taking appropriate personnel action against such an employee, up to and including termination; or

(2) Requiring such employee to participate satisfactorily in a drug abuse assistance or rehabilitation program approved for such purposes by a Federal, State, or Local health, Law enforcement, or other appropriate agency;

(g) Making a good faith effort to continue to maintain a drug-free workplace through implementation of paragraphs (a), (b), (c), (d), (e), and (f).

B. The grantee shall insert in the space provided below the site(s) for the performance or work done in connection with the specific grant: Place of Performance (Street address, city, county, state, zip code)

_____

_____

Check ____ if there are workplaces on file that are not identified here.

II. GRANTEES WHO ARE INDIVIDUALS

The grantee certifies that, as a condition of the grant, he or she will not engage in the unlawful manufacture, distribution, dispensing, possession or use of a controlled substance in conducting any activity with the grant.

_____

Organization Name AO or NRA Number and Title

_____

Printed Name and Title of Authorized Representative

_____

Signature Date

_____

Printed Principal Investigator Name Proposal Title

FORM E

CERTIFICATION REGARDING
DEBARMENT, SUSPENSION, AND OTHER RESPONSIBILITY MATTERS
PRIMARY COVERED TRANSACTIONS

This certification is required by the regulations implementing Executive Order 12549, Debarment and Suspension, 34 CFR Part 85, Section 85.510, Participants' responsibilities. The regulations were published as Part VII of the May 28, 1988 Federal Register (pages 19160-19211). Copies of the regulations may be obtained by contacting the U.S. Department of Education, Grants and Contracts Service, 400 Maryland Avenue, S.W. (Room 3633 GSA Regional Office Building No. 3), Washington, D.C. 20202-4725, telephone (202) 732-2505.

A. The applicant certifies that it and its principals:

(a) Are not presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from covered transactions by any Federal department or agency;

(b) Have not within a three-year period preceding this application been convicted or had a civil judgement rendered against them for commission of fraud or a criminal offense in connection with obtaining, attempting to obtain, or performing a public (Federal, State, or Local) transaction or contract under a public transaction; violation of Federal or State antitrust statutes or commission of embezzlement, theft, forgery, bribery, falsification or destruction of records, making false statements, or receiving stolen property;

(c) Are not presently indicted for or otherwise criminally or civilly charged by a government entity (Federal, State, or Local) with commission of any of the offenses enumerated in paragraph A.(b) of this certification; and

(d) Have not within a three-year period preceding this application/proposal had one or more public transactions (Federal, State, or Local) terminated for cause or default; and

B. Where the applicant is unable to certify to any of the statements in this certification, he or she shall attach an explanation to this application.

C. Certification Regarding Debarment, Suspension, Ineligibility and Voluntary Exclusion - Lowered Tier Covered Transactions (Subgrants or Subcontracts)

(a) The prospective lower tier participant certifies, by submission of this proposal, that neither it nor its principles is presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from participation in this transaction by any Federal department of agency.

(b) Where the prospective lower tier participant is unable to certify to any of the statements in this certification, such prospective participant shall attach an explanation to this proposal.

_____

Organization Name AO or NRA Number and Title

_____

Printed Name and Title of Authorized Representative

_____

Signature Date

_____

Printed Principal Investigator Name Proposal Title

FORM F

CERTIFICATION REGARDING LOBBYING

As required by S 1352 Title 31 of the U.S. Code for persons entering into a grant or cooperative agreement over $100,000, the applicant certifies that:

(a) No Federal appropriated funds have been paid or will be paid by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, in connection with making of any Federal grant, the entering into of any cooperative, and the extension, continuation, renewal, amendment, or modification of any Federal grant or cooperative agreement;

(b) If any funds other than Federal appropriated funds have been paid or will be paid to any person for influencing or attempting an officer or employee of any agency, Member of Congress, an or an employee of a Member of Congress in connection with this Federal grant or cooperative agreement, the undersigned shall complete Standard Form - LLL, "Disclosure Form to Report Lobbying," in accordance with its instructions.

(c) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers (including subgrants, contracts under grants and cooperative agreements, and subcontracts), and that all subrecipients shall certify and disclose accordingly.

This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into this transaction imposed by S1352, title 31, U.S. Code. Any person who fails to file the required certification shall be subject to a civil penalty of not less than $10,000 and not more than $100,000 for each such failure.

Organization Name AO or NRA Number and name

Printed Name and Title of Authorized Representative

Signature Date

Printed Principal Investigator Name Proposal Title

NASA Research Announcement (NRA) Mailing List Update

*This is the form to update information for the NASA Office of Life & Microgravity Sciences & Applications (OLMSA) NRA mailing list. Please fill out **CONTACT INFORMATION** completely. Check only those that apply in **INSTITUTION TYPE** and **PROGRAM AREAS/DISCIPLINES.***
Fold the form, secure with tape (do not staple), and mail it back to the address on the reverse side. Proper postage must be applied.

Mailing Label Updates may be submitted electronically via E-Mail or World Wide Web to the following addresses:

Check one:

- ☐ 1. Please **add** my name to the mailing list.
- ☐ 2. Please **remove** my name from the mailing list (please attach mailing label).
- ☐ 3. Please **change** my current listing (please attach mailing label).
- ☐ 4. Please leave my current listing **unchanged** (please attach mailing label).

Contact Information

If your address has changed or your mailing label is incorrect, please provide COMPLETE contact information.

Prefix: (Mr., Mrs., Ms., Dr., Prof., etc.)

Suffix: (M.D., Ph.D., Jr., III, etc.)

Name, First:

Last:

Position Title:

Mail Code, Loc:

Office, Dept, Div:

Org/Agency/Ctr, Univ:

Street or PO Box:

City:

State:

Zip Code:

Country:

Telephone No:

Fax No:

Internet/E-Mail:

Institution Type

(check all that apply)

- ☐ 1. College or University
- ☐ 2. Minority College or University
- ☐ 3. Minority Business
- ☐ 4. NASA Center
- ☐ 5. Other Government Agency
- ☐ 6. Nonprofit Corporation
- ☐ 7. Small Business
- ☐ 8. Private Industry
- ☐ 9. Foreign Addressee

Program Areas/Disciplines

(check main area of interest)

☐ **1. Life Sciences**

- ☐ A. Advanced Life Support
- ☐ B. Advanced Technology Development
- ☐ C. Data Analysis
- ☐ D. Environmental Health
- ☐ E. Space Biology
- ☐ F. Space Human Factors
- ☐ G. Space Physiology & Countermeasures
- ☐ H. Space Radiation Health

☐ **2. Microgravity Sciences**

- ☐ A. Biotechnology
- ☐ B. Combustion Science
- ☐ C. Fluid Physics
- ☐ D. Materials Science
- ☐ E. Microgravity Physics

☐ Please send me notifications of announcements via E-Mail only.

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SUITE 801
WASHINGTON, DC 20024

NASA OFFICIAL MAILING LIST UPDATE

ATTACHMENT

This attachment is not part of the preceding NASA Research Announcement (NRA). It is a notification that opportunities exist for proposals which predominantly feature applied commercial research and must have an industrial cost sharing partner.

Office of Space Access and Technology, Space Processing Division

Notice of Areas of Interest for

Biotechnology Applied Research for the Commercial Development of Space Program

In July of 1994, the NASA Administrator signed the *Agenda for Change* which challenges NASA to change the way it conducts business and emphasizes the importance of the Commercial Technology Mission. As a result, the Office of Space Access and Technology (OSAT) encourages proposers to address objectives in commercial research. NASA seeks and encourages, to the maximum extent possible, the fullest commercial use of space. The OSAT Space Processing program focuses on the use of space for developing commercial processes, products and/or services by industry with the goals of (1) Fostering the development of new processes, products and services using the attributes of space and space technology, (2) Increasing U.S. business participation in space enterprise, (3) Providing the opportunity for students to engage with industry in space program activities, and (4) Facilitating mutually beneficial international partnerships with industry to expand commercial use of space.

Submission and Scope of Proposal

Proposals selected in response to this announcement benefit from; (a) the expertise and support of the NASA Centers for the Commercial Development of Space, and of NASA, (b) the fact that NASA, to foster these developmental, high risk activities, does not charge for transportation to space unless a profit is expected, and (c) the participants may retain certain proprietary rights.

The space processing program uses industry requirements as the basis for commercial technology development, prototyping, and demonstration. Proposals must be submitted to an appropriate Center for Commercial Development of Space. Proposals submitted for unspecified hardware or general support facilities should apply to the CCDS with the appropriate area of expertise as identified in the following list. **Please note that hardware and facility availability is subject to negotiation through the CCDS.**

Center for Bioserve Space Technologies
Areas: Fluid Bioprocessing, Immune Systems, Biomaterials Development, Physiological Models, Controlled Agricultural Systems

University of Colorado-Boulder
Department of Aerospace Engineering Sciences
Campus Box 429
Boulder, Colorado 80309
Director: Dr. George W. Morganthaler
(303) 492-3633
fax: (303) 492-8883

Center for Macromolecular Crystallography
Areas: Protein Crystal Growth, Enhanced Drug Design Techniques, Processing of Protein Materials On-orbit Analysis of Protein Structure and Crystal Configurations, Protein Structure Modelling

University of Alabama-Birmingham
Box 79-THT, UAB Station
Birmingham, AL 35294-0005
Director: Dr. Lawrence DeLucas
(205) 934-5329
fax: (205) 934-0484

Consortium for Materials Development in Space

Areas: Metal Sintering, Metal Electrodeposition, Non-Linear Optical Materials, Polymer Foams, Atomic Oxygen, Space Experiment Furnace, Accelerometers, Implant Technology Electrodeposition, Materials Dispersions, Organic Separations

University of Alabama -Huntsville
Research Institute Building/M-65
301 Sparkman Drive
Huntsville, AL 35899
Director: Dr. Charles Lundquist
(205) 895-6620
fax: (205) 895-6791

Proposals should be submitted to one of the three Centers for Commercial Development of Space (CCDS) listed above. Proposal submission is limited to only one CCDS. The CCDS's were established in 1985 and are consortia of government, academia, and industry conducting space-related research with commercial potential. NASA provides access to space and contributes to the organizational costs of each CCDS. The CCDS's secure additional funding through partnerships with industrial affiliates. The CCDS's can also assist the private sector with insights as to the benefits of applying space-based knowledge or capabilities to the solution of problems, the aquisition of new data and techniques, the development of new capabilities, and the means of accomplishing spaceflight activities. These are all aimed towards exploiting the characteristics of space flight for the development of new commercially viable products, processes, industries, and markets.

These proposals must include the envisioned product developed using the research results, the projected market for the product research, and the private sector resources committed for the research effort. Areas of focus are those areas in the field of Biotechnology which correspond to the areas of expertise of individual CCDS's. Flight hardware capability should be used by researchers for consideration for part of proposal generation. However, proposers may also submit hardware they have developed as part of the proposal. General questions regarding proposals should be addressed to the appropriate CCDS.

Selection Criterion

Evaluation will be conducted by and selections made by CCDS's. Since the goal of the Space Processing Program is to foster the use of space for commercial products and services, support for research activity depends upon the envisioned product and its commercial potential and impact. In order to be selected through the appropriate CCDS, **each product must meet the following five criteria:**

First Criterion: Technical assessment

- The need for space flight is clearly defined and justified
- The technical approach is feasible and supports development of the product

Second Criterion: Business plan

- A non-U.S. Government market is defined and of sufficient size
- There is evidence that the proposed process or product better meets the target market
- There is a commercial affiliate(s) to provide evidence of necessary resources, capability, planning, and experience to bring the product to market
- The proposed space activity is essential to product development and is consistent with business planning
- A roadmap exists that includes the essential activities to bring the product to market beyond the space development activities
- Significant private resources (financial and in-kind) are at risk

Third Criterion: Space Access

- The required flight opportunities exist and can accommodate stated research
- The space research requirements are consistent with potential product benefits

Fourth Criterion: Funding Adequacy

- Funding requirements are identified and justified
- The commercial affiliate provides evidence of funding commitment for the research program

- Government funding is available and consistent with required commitment

Fifth Criterion: International Collaborators

- An agreement exists which clearly demonstrates the benefit of the activity to the U.S. taxpayer

Proposal Outline

To facilitate coordination and review, the following is the suggested outline for proposal submission. It is requested that the proposals contain this information and in the format shown below:

-Title Page
-Table of Contents
- One Page White Paper Overview including:
    -Concept
    -Objectives
    -Approach (including space flight requirements)
    -Hardware (development or usage)
- Executive Summary
-Commercial Product Description
-Justification (see criteria)
    -Technical Assessment
    -Business Plan
    -Space Access
    -Funding Adequacy

The proposal should not exceed 20 pages in length, exclusive of appendices and supplementary material, and should be typed on 8-1/2 x 11 inch paper with a 10- or 12-point font.

Five copies of the proposal must be received by the appropriate CCDS by August 27, 1996, to assure full consideration. Proposal submission is limited to only one CCDS per proposal.

Proposal Evaluation

The initial proposal assessment is based on technical assessment/business plan merit, compliance with the selection criteria, fit with ongoing programs, potential availability of hardware, funds, and flight opportunities. This assessment will provide the basis for any future discussions or negotiations between the proposer and the CCDS. Please note that, after discussion with the proposer, a CCDS may reject the proposal or take other actions including suggesting referral to another CCDS.

It should be noted that industrial participants are cost sharing partners and support all phases of the process from developing initial requirements to implementation of final results. It should further be noted that increased funding will not necessarily be available for the CCDS as a result of a collaboration associated with this NASA Notice. However, the degree and amount of proposed investment, in addition to the suitability of the content of the proposal, could generate interest in the revaluation of programs and priorities. It is to be understood that all selected proposals are to be negotiated directly between the proposers and CCDS.